

=> fil biotechno;d que 13  
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FILE LAST UPDATED: 7 NOV 2002 <20021107/UP>  
FILE COVERS 1980 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN  
/CT AND BASIC INDEX <<<

L1 117 SEA FILE=BIOTECHNO ABB=ON TOMLINSON I?/AU  
L2 17 SEA FILE=BIOTECHNO ABB=ON HOLT L?/AU  
L3 2 SEA FILE=BIOTECHNO ABB=ON L1 AND L2

*inventor  
search*

=> fil biotechds; d que 136; d que 147

FILE 'BIOTECHDS' ENTERED AT 10:56:34 ON 12 NOV 2002  
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FILE LAST UPDATED: 7 NOV 2002 <20021107/UP>

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L36 0 SEA FILE=BIOTECHDS ABB=ON HOLT L?/AU

L35 7 SEA FILE=BIOTECHDS ABB=ON TOMLINSON I?/AU  
L37 4350 SEA FILE=BIOTECHDS ABB=ON MICROARRAY# OR ARRAY# OR BIOCHIP#  
OR BIO CHIP#  
L38 8801 SEA FILE=BIOTECHDS ABB=ON REPERTOIRE# OR LIBRAR?  
L47 4 SEA FILE=BIOTECHDS ABB=ON L35 AND (L37 OR L38)

=> fil capl; d que 155

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FILE COVERS 1907 - 12 Nov 2002 VOL 137 ISS 20  
FILE LAST UPDATED: 11 Nov 2002 (20021111/ED)

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L53 ( 135)SEA FILE=CAPLUS ABB=ON TOMLINSON I?/AU  
L54 ( 331)SEA FILE=CAPLUS ABB=ON HOLT L?/AU  
L55 7 SEA FILE=CAPLUS ABB=ON L53 AND L54

=> fil wpids; d que 1110

FILE 'WPIDS' ENTERED AT 10:56:37 ON 12 NOV 2002  
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FILE LAST UPDATED: 8 NOV 2002 <20021108/UP>  
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L108( 19)SEA FILE=WPIDS ABB=ON TOMLINSON I?/AU  
L109( 46)SEA FILE=WPIDS ABB=ON HOLT L?/AU  
L110 3 SEA FILE=WPIDS ABB=ON L108 AND L109

=> fil biosis; d que 1143

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CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNS) PRESENT  
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 7 November 2002 (20021107/ED)

L141( 215)SEA FILE=BIOSIS ABB=ON TOMLINSON I?/AU  
L142( 176)SEA FILE=BIOSIS ABB=ON HOLT L?/AU  
L143 1 SEA FILE=BIOSIS ABB=ON L141 AND L142

=> dup rem 155,1143,13,147,1110

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PROCESSING COMPLETED FOR L143  
PROCESSING COMPLETED FOR L3  
PROCESSING COMPLETED FOR L47  
PROCESSING COMPLETED FOR L110  
L163 12 DUP REM L55 L143 L3 L47 L110 (5 DUPLICATES REMOVED)  
ANSWERS '1-7' FROM FILE CAPLUS  
ANSWER '8' FROM FILE BIOTECHNO  
ANSWERS '9-12' FROM FILE BIOTECHDS

=> d ibib ab 1163 1-12

L163 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1  
ACCESSION NUMBER: 2001:935822 CAPLUS  
DOCUMENT NUMBER: 136:34329  
TITLE: Matrix screening method to detect interactions  
INVENTOR(S): Holt, Lucy Jessica; Tomlinson, Ian  
PATENT ASSIGNEE(S): Diversys Limited, UK  
SOURCE: PCT Int. Appl., 42 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001098534	A2	20011227	WO 2001-GB2831	20010622
WO 2001098534	A3	20020530		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,  
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,  
UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2000-15443 A 20000623  
GB 2000-26099 A 20001025  
US 2000-246851P P 20001108

AB The invention concerns a method which can be used to screen two or more repertoires of mols. against one another and/or to create combinatorial repertoires by combining two or more repertoires. In particular, the invention relates to a method whereby two repertoires of mols. can be screened such that substantially all members of the first repertoire are tested against substantially all members of the second repertoire for functional interactions. Furthermore, the invention relates to the creation and screening of antibody repertoires by combining a repertoire of heavy chains with a repertoire of light chains such that antibodies formed by the substantially all combinations of heavy and light chains can

be screened against one or more target ligands.

L163 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2  
ACCESSION NUMBER: 2001:417259 CAPLUS  
DOCUMENT NUMBER: 135:30956  
TITLE: Direct screening method for polypeptides and other  
target ligands using in situ expressed arrays of  
polypeptides or antibodies  
INVENTOR(S): **Holt, Lucy Jessica**; De Wildt, Rudolf Maria  
Theodora; **Tomlinson, Ian**  
PATENT ASSIGNEE(S): Diversys Limited, UK  
SOURCE: PCT Int. Appl., 59 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001040803	A1	20010607	WO 2000-GB4638	20001204
W:				
AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				
CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,				
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,				
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,				
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,				
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,				
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,				
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1242821	A1	20020925	EP 2000-977784	20001204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, IE, SI,				
LT, LV, FI, RO, MK, CY, AL				
NO 2002002312	A	20020603	NO 2002-2312	20020515
PRIORITY APPLN. INFO.:			GB 1999-28787	A 19991203
			WO 2000-GB4638	W 20001204

AB The invention concerns a method for screening a repertoire of polypeptides to identify one or more members that interact with one or more target mols., comprising: (a) immobilizing the target mol.(s) on a support; (b) arranging a plurality of nucleic acid mols. encoding the repertoire of polypeptides in an array; (c) juxtaposing the target mol.(s) and the arrayed nucleic acid mols.; (d) expressing the arrayed nucleic acid mols. to produce the polypeptides such that said polypeptides come into contact with the target mol.(s) on the support and a subset of the polypeptides interacts with the target mols.; and (e) detecting the interaction of the polypeptides with the target mols. on the support. The invention also provides a high d. antibody array consisting of thousands of different polypeptide features, spatially arranged on a solid support for screening against different target ligands.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L163 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3  
ACCESSION NUMBER: 2001:417020 CAPLUS  
DOCUMENT NUMBER: 135:30972  
TITLE: Naive polypeptide screening method using target ligand  
INVENTOR(S): **Holt, Lucy Jessica**; De Wildt, Rudolf Maria  
Theodora; **Tomlinson, Ian**  
PATENT ASSIGNEE(S): Diversys Limited, UK  
SOURCE: PCT Int. Appl., 41 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001040312	A2	20010607	WO 2000-GB4629	20001204
WO 2001040312	A3	20020117		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001017187	A5	20010612	AU 2001-17187	20001204
EP 1234179	A2	20020828	EP 2000-979803	20001204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.: GB 1999-28789 A 19991203 WO 2000-GB4629 W 20001204				
AB The invention describes a method for isolating, from a naive polypeptide repertoire which has not been preselected with a specific target ligand, a polypeptide of interest capable of interacting with said specific target ligand, which method comprises direct screening of the naive polypeptide repertoire with the target ligand in order to identify the polypeptide of interest. An expressed cDNA array was screened using antibodies as target ligands.				
L163 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 4				
ACCESSION NUMBER: 2000:757587 CAPLUS				
DOCUMENT NUMBER: 134:40699				
TITLE: The use of recombinant antibodies in proteomics				
AUTHOR(S): Holt, Lucy J.; Enever, Carolyn; De Wildt, Ruud M. T.; Tomlinson, Ian M.				
CORPORATE SOURCE: MRC Laboratory of Molecular Biology and MRC Centre for Protein Engineering, Cambridge, CB2 2QH, UK				
SOURCE: Current Opinion in Biotechnology (2000), 11(5), 445-449 CODEN: CUOBE3; ISSN: 0958-1669				
PUBLISHER: Elsevier Science Ltd.				
DOCUMENT TYPE: Journal; General Review				
LANGUAGE: English				
AB A review with 49 refs. Recombinant antibodies are becoming increasingly important in the field of proteomics. Recent advances include the development of large phage-antibody libraries that contain high-affinity binders to almost any target protein, and new methods for high-throughput selection of antibody-antigen interactions. Coupled with a range of new screening technologies that use high-d. antibody arrays to identify differentially expressed proteins, these antibody libraries can be applied to whole proteome anal.				
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT				
L163 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2002 ACS				
ACCESSION NUMBER: 2002:638192 CAPLUS				
DOCUMENT NUMBER: 137:152050				
TITLE: Matrix screening method to detect interactions				
INVENTOR(S): Tomlinson, Ian; Holt, Lucy J.				
PATENT ASSIGNEE(S): UK				
SOURCE: U.S. Pat. Appl. Publ., 43 pp., Cont.-in-part of U.S. Ser. No. 888,313.				

DOCUMENT TYPE: CODEN: USXXCO  
LANGUAGE: Patent  
FAMILY ACC. NUM. COUNT: English 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002115068	A1	20020822	US 2001-8571	20011203
US 2002055110	A1	20020509	US 2001-888313	20010622
PRIORITY APPLN. INFO.:			GB 2000-15443	A 20000623
			GB 2000-26099	A 20001025
			US 2000-246851P	P 20001108
			US 2001-888313	A2 20010622

AB The invention concerns a method which can be used to screen two or more repertoires of mols. against one another and/or to create combinatorial repertoires by combining two or more repertoires. In particular, the invention relates to a method whereby two repertoires of mols. can be screened such that all members of the first repertoire are tested against all members of the second repertoire for functional interactions. Furthermore, the invention relates to the creation and screening of antibody repertoires by combining a repertoire of heavy chains with a repertoire of light chains such that antibodies formed by the all combinations of heavy and light chains can be screened against one or more target ligands.

L163 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:217551 CAPLUS  
DOCUMENT NUMBER: 135:164199  
TITLE: Protein profiling comes of age  
AUTHOR(S): Tomlinson, Ian M.; Holt, Lucy J.  
CORPORATE SOURCE: MRC Laboratory of Molecular Biology and MRC Centre for Protein Engineering, Cambridge, CB2 2QH, UK  
SOURCE: GenomeBiology [online computer file] (2001), 2(2), No pp. given  
CODEN: GNBLEW; ISSN: 1465-6914  
URL: <http://www.genomebiology.com/retriever.asp?url=/2001/2/2/reviews/1004>  
PUBLISHER: BioMed Central Ltd.  
DOCUMENT TYPE: Journal; General Review; (online computer file)  
LANGUAGE: English

AB A review with 28 refs. Ever since DNA microarrays were first applied to the quantitation of RNA levels, there has been considerable interest in generating a protein homolog that can be used to assay cellular protein expression. A recent paper describes the first microarray that can be used for such protein profiling.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L163 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:636966 CAPLUS  
DOCUMENT NUMBER: 133:280237  
TITLE: By-passing selection: direct screening for antibody-antigen interactions using protein arrays  
AUTHOR(S): Holt, Lucy J.; Bussow, Konrad; Walter, Gerald; Tomlinson, Ian M.  
CORPORATE SOURCE: MRC Lab. for Molecular Biology and MRC Centre for Protein Engineering, Cambridge, CB2 2QH, UK  
SOURCE: Nucleic Acids Research (2000), 28(15), e72, ii-v  
CODEN: NARHAD; ISSN: 0305-1048  
PUBLISHER: Oxford University Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The authors have developed a system to identify highly specific antibody-antigen interactions by protein array screening. This removes the need for selection using animal immunization or in vivo techniques such as phage or ribosome display. The authors screened an array of 27,648 human fetal brain proteins with 12 well-expressed antibody fragments that had not previously been exposed to any antigen. Four highly specific antibody-antigen pairs were identified, including three antibodies that bind proteins of unknown function. The target proteins were expressed at a very low copy no. on the array, emphasizing the unbiased nature of the screen. The specificity and sensitivity of binding demonstrates that this 'naive' screening approach could be applied to the high throughput isolation of specific antibodies against many different targets in the human proteome.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L163 ANSWER 8 OF 12 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.

ACCESSION NUMBER: 2001:32186044 BIOTECHNO  
TITLE: Protein profiling comes of age  
AUTHOR: Tomlinson I.M.; Holt L.J.  
CORPORATE SOURCE: I.M. Tomlinson, MRC Laboratory of Molecular Biology,  
MRC Centre for Protein Engineering, Hills Road,  
Cambridge CB2 2QH, United Kingdom.  
E-mail: imt@mrc-lmb.cam.ac.uk  
SOURCE: GenomeBiology, (2001), 2/2 (1004.1-1004.3), 28  
reference(s)  
CODEN: GNBFW ISSN: 1465-6906  
DOCUMENT TYPE: Journal; General Review  
COUNTRY: United Kingdom  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB Ever since DNA microarrays were first applied to the quantitation of RNA levels, there has been considerable interest in generating a protein homolog that can be used to assay cellular protein expression. A recent paper describes the first microarray that can be used for such protein profiling.

L163 ANSWER 9 OF 12 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

ACCESSION NUMBER: 1999-08693 BIOTECHDS  
TITLE: Screening for functional polypeptides which bind a ligand;  
drug screening using phage display  
AUTHOR: Tomlinson I; Winter G  
PATENT ASSIGNEE: Med.Res.Counc.  
LOCATION: London, UK.  
PATENT INFO: WO 9920749 29 Apr 1999  
APPLICATION INFO: WO 1998-GB3135 20 Oct 1998  
PRIORITY INFO: US 1997-66729 21 Nov 1997; GB 1997-22131 20 Oct 1997  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 1999-288302 [24]

AB A new method for screening for functional proteins which bind a ligand involves contacting a **repertoire** of proteins with a generic ligand and then screening selected functional proteins with a target ligand. The method for selecting, from a **repertoire** of proteins, a population of functional proteins which bind a target ligand in a 1st binding site and a generic ligand in a 2nd binding site, which generic ligand is capable of binding functional members of the **repertoire** regardless of target specificity involves: contacting the **repertoire** with the generic ligand and selecting functional proteins bound to it; and contacting the selected functional proteins with the target ligand and selecting a population of proteins which bind to the target ligand. Also claimed are: a **library** where the functional members have binding sites for both generic and target

ligands; a **library** for selection with both generic and target ligands; and a nucleic acid **library** encoding a **library** of proteins. The method allows removal of non-functional proteins and enrichment of chosen **repertoire** of proteins, which are used in diagnosis, prophylaxis, and therapy. (67pp)

L163 ANSWER 10 OF 12 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

ACCESSION NUMBER: 1994-11604 BIOTECHDS

TITLE: Isolation of high affinity human antibodies directly from large synthetic **repertoires**; antibody engineering by combinatorial gene bank peptide **library** phage display

AUTHOR: Griffiths A D; Williams S C; Hartley O; Tomlinson I M; Waterhouse P; Crosby W L

CORPORATE SOURCE: Med.Res.Counc.; Imperial-Cancer-Res.Fund; Cambridge-Antibody-Technol.

LOCATION: MRC Centre for Protein Engineering, Hills Road, Cambridge CB2 2QH, UK.

SOURCE: EMBO J.; (1994) 13, 14, 3245-60

CODEN: EMJODG

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In a new method, high-affinity human recombinant antibodies were isolated directly from large **repertoires**. Highly diverse **repertoires** of heavy and light chains were constructed entirely in vitro from a bank of human variable gene segments and, by recombination in *Escherichia coli*, a large (6,500 million) synthetic **repertoire** of Fab fragments was generated, displayed on filamentous phage fd. From this **repertoire**, Fab fragments were isolated which bound to a range of different antigens and haptens (including fluorescein, serum albumin, tubulin, calmodulin, rape (*Brassica napus*) acetolactate-synthase (EC-4.1.3.18), *E. coli* maltose binding protein, tissue plasminogen-activator (EC-3.4.21.68), urokinase (3.4.12.73), plasmin (EC-3.4.21.7), carcinoembryonic antigen, ferritin light chain, etc.) with affinities comparable to those of antibodies from a secondary immune response in mice (up to 4 nM). Although the VH-26 (DP-47) segment was the most commonly used segment in both artificial and natural **repertoires**, there were also major differences in the pattern of segment usage. (81 ref)

L163 ANSWER 11 OF 12 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

ACCESSION NUMBER: 1994-03874 BIOTECHDS

TITLE: Antibody fragments from a 'single pot' phage display **library** as immunochemical reagents; gene bank application in antibody, monoclonal antibody, single chain antibody or Fv fragment production

AUTHOR: Nissim A; Hoogenboom H R; Tomlinson I M; Flynn G; Midgley C; Lane D

CORPORATE SOURCE: MRC-Cent.Protein-Eng.; Cambridge-Antibody-Technol.

LOCATION: MRC Centre for Protein Engineering, Hills Road, Cambridge, CB2 2QH, UK.

SOURCE: EMBO J.; (1994) 13, 3, 692-98

CODEN: EMJODG

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The display of **repertoires** of antibody fragments on the surface of filamentous phages offers a new method for production of antibodies with predefined binding specificities. The technology was used to make immunochemical reagents to a range of antigens by selection from a **repertoire** of over 100 million clones made in vitro from human V gene segments. From the same 'single pot' **repertoire**, phage were isolated with binding activities to each of 18 antigens, including the intracellular protein p53, elongation factor EF-1-alpha,



immunoglobulin binding protein, rhombotin-2 oncogene protein and sex determining region Y protein. Both phage and single chain Fv fragments secreted from the infected bacteria were used as monoclonal antibody and polyclonal antibody reagents in Western blots. The monoclonal reagents were used for epitope mapping (in which a new epitope of p53 was identified) and for cell staining. The antibody reagents for research can be derived from 'single pot' phage display gene banks. (51 ref)

L163 ANSWER 12 OF 12 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

ACCESSION NUMBER: 1994-14066 BIOTECHDS

TITLE: Antibody fragments from a 'single pot' phage display  
**library** as immunochemical reagents;  
monoclonal antibody engineering (conference abstract)

AUTHOR: Nissim A; Hoogenboom H R; Tomlinson I M; Flynn G;  
Midgley C; Lane D

CORPORATE SOURCE: Med.Res.Counc.

LOCATION: MRC Centre for Protein Engineering, Hills Road, Cambridge,  
CB2 2QH, UK.

SOURCE: J.Cell.Biochem.; (1994) Suppl.18D, 203  
CODEN: JCEBD5

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Phage display technology was used to produce immunochemical reagents to a range of antigens by selection from a **repertoire** of over 100 million clones produced in vitro from human variable region segments. From the same 'single pot' **repertoire**, phages were isolated with binding activities to each of 18 antigens, including the intracellular proteins p53, elongation factor EF-1-alpha, Ig binding protein, rhombotin-2 oncogene protein and sex determining region Y-protein. Both phages and Fv single chain antibody fragments secreted from infected bacteria were used as polyclonal and monoclonal antibody reagents in Western blots. The monoclonal antibodies were used for epitope mapping (allowing identification of a new epitope of p53) and for staining of cells. This shows that antibody reagents for research can be readily derived from 'single pot' phage display **libraries**. (0 ref)

=> fil biotechno

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search*

=> d que l15; d que l26; d que l34

L4 32829 SEA FILE=BIOTECHNO ABB=ON LIBRAR?  
L5 11373 SEA FILE=BIOTECHNO ABB=ON MICROARRAY? OR ARRAY? OR BIOCHIP#  
OR BIO CHIP#  
L6 5653 SEA FILE=BIOTECHNO ABB=ON REPERTOIRE#  
L7 1261 SEA FILE=BIOTECHNO ABB=ON JUXTAPOS?  
L8 25076 SEA FILE=BIOTECHNO ABB=ON CHANNEL?  
L9 561 SEA FILE=BIOTECHNO ABB=ON ETCH?  
L10 828 SEA FILE=BIOTECHNO ABB=ON PERPENDICULAR?  
L14 6845 SEA FILE=BIOTECHNO ABB=ON (SODIUM OR ION OR CHLORIDE) (W) L8  
L15 6 SEA FILE=BIOTECHNO ABB=ON L5 AND (L4 OR L6) AND (L8 OR L9 OR  
L10 OR L7) NOT L14

L4 32829 SEA FILE=BIOTECHNO ABB=ON LIBRAR?  
L5 11373 SEA FILE=BIOTECHNO ABB=ON MICROARRAY? OR ARRAY? OR BIOCHIP#  
OR BIO CHIP#  
L6 5653 SEA FILE=BIOTECHNO ABB=ON REPERTOIRE#  
L17 2807 SEA FILE=BIOTECHNO ABB=ON TWO(1W)MORE  
L25 565 SEA FILE=BIOTECHNO ABB=ON PROCESS OPTIMIZATION/CT  
L26 1 SEA FILE=BIOTECHNO ABB=ON L5 AND (L4 OR L6) AND L17 AND L25

L4 32829 SEA FILE=BIOTECHNO ABB=ON LIBRAR?  
L5 11373 SEA FILE=BIOTECHNO ABB=ON MICROARRAY? OR ARRAY? OR BIOCHIP#  
OR BIO CHIP#  
L6 5653 SEA FILE=BIOTECHNO ABB=ON REPERTOIRE#  
L16 29680 SEA FILE=BIOTECHNO ABB=ON FIRST AND SECOND  
L17 2807 SEA FILE=BIOTECHNO ABB=ON TWO(1W)MORE  
L20 19 SEA FILE=BIOTECHNO ABB=ON L5 AND (L4 OR L6) AND (L16 OR L17)  
L33 792 SEA FILE=BIOTECHNO ABB=ON GRID#  
L34 1 SEA FILE=BIOTECHNO ABB=ON L20 AND L33

=> s (l15 or l26 or l34) not l3

L164 8 (L15 OR L26 OR L34) NOT L3

*previously  
printed w/ inventor search*

=> fil biotechds; d que l52

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FILE LAST UPDATED: 7 NOV 2002

<20021107/UP>

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>>> NEW CLASSIFICATION SYSTEM FROM 2002 ONWARDS - SEE HELP CLA <<<

L37 4350 SEA FILE=BIOTECHDS ABB=ON MICROARRAY# OR ARRAY# OR BIOCHIP#  
OR BIO CHIP#  
L38 8801 SEA FILE=BIOTECHDS ABB=ON REPERTOIRE# OR LIBRAR?  
L39 93 SEA FILE=BIOTECHDS ABB=ON JUXTAPOS?  
L40 218 SEA FILE=BIOTECHDS ABB=ON GRID?  
L41 167 SEA FILE=BIOTECHDS ABB=ON PERPENDICULAR?  
L42 216 SEA FILE=BIOTECHDS ABB=ON ETCH?  
L43 1782 SEA FILE=BIOTECHDS ABB=ON CHANNEL?  
L44 359 SEA FILE=BIOTECHDS ABB=ON (SODIUM OR CHLORIDE OR ION OR  
ANION) (W) L43  
L48 16 SEA FILE=BIOTECHDS ABB=ON L37 AND L38 AND ((L39 OR L40 OR L41  
OR L42) OR (L43 NOT L44))  
L51 1708 SEA FILE=BIOTECHDS ABB=ON "BIOCHIPS AND BIOARRAYS"/CC  
L52 5 SEA FILE=BIOTECHDS ABB=ON L48 AND L51

=> s 152 not 147

L165

5 L52 NOT

(L47) *previously printed*

=> fil capl

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FILE COVERS 1907 - 12 Nov 2002 VOL 137 ISS 20  
FILE LAST UPDATED: 11 Nov 2002 (20021111/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> d que 1107; d que 194; d que 182; d que 173; d que 167; d que 163

L95 ( 9707)SEA FILE=CAPLUS ABB=ON LIBRARY/CW  
L96 ( 541)SEA FILE=CAPLUS ABB=ON CMBI/RL  
L97 ( 8247)SEA FILE=CAPLUS ABB=ON MICROARRAY?/OBI OR BIOCHIP?/OBI  
L98 ( 8021)SEA FILE=CAPLUS ABB=ON REPERTOIR?  
L99 ( 1128901)SEA FILE=CAPLUS ABB=ON INTERACT?  
L100 ( 27)SEA FILE=CAPLUS ABB=ON (L95 OR L96 OR L98) AND L97(L) L99  
L101 ( 22)SEA FILE=CAPLUS ABB=ON 9/SC, SX AND L100  
L102 ( 165038)SEA FILE=CAPLUS ABB=ON FIRST AND SECOND  
L103 ( 1867673)SEA FILE=CAPLUS ABB=ON TWO OR MULTIPLE  
L104 ( 856371)SEA FILE=CAPLUS ABB=ON SEVERAL  
L105 ( 18)SEA FILE=CAPLUS ABB=ON L101 AND (L102 OR L103 OR L104)

*- section code 9 = Biochemical methods*

L106 ( 5702) SEA FILE=CAPLUS ABB=ON TWO HYBRID  
L107 4 SEA FILE=CAPLUS ABB=ON L105 NOT L106

L83 ( 9707) SEA FILE=CAPLUS ABB=ON LIBRARY/CW  
L84 ( 541) SEA FILE=CAPLUS ABB=ON CMBI/RL  
L85 ( 266991) SEA FILE=CAPLUS ABB=ON CHANNEL?  
L86 ( 168613) SEA FILE=CAPLUS ABB=ON ETCH?  
L87 ( 8247) SEA FILE=CAPLUS ABB=ON MICROARRAY?/OBI OR BIOCHIP?/OBI  
L88 ( 8021) SEA FILE=CAPLUS ABB=ON REPERTOIR?  
L89 ( 4201) SEA FILE=CAPLUS ABB=ON JUXTAPOS?  
L90 ( 1128901) SEA FILE=CAPLUS ABB=ON INTERACT?  
L91 ( 7) SEA FILE=CAPLUS ABB=ON L88 AND L87 AND ((L85 OR L86) OR L89  
OR L90)  
L92 ( 27) SEA FILE=CAPLUS ABB=ON (L83 OR L84 OR L88) AND L87(L) L90  
L93 ( 22) SEA FILE=CAPLUS ABB=ON 9/SC, SX AND L92  
L94 3 SEA FILE=CAPLUS ABB=ON L91 AND L93

L74 ( 9707) SEA FILE=CAPLUS ABB=ON LIBRARY/CW  
L75 ( 541) SEA FILE=CAPLUS ABB=ON CMBI/RL  
L76 ( 8247) SEA FILE=CAPLUS ABB=ON MICROARRAY?/OBI OR BIOCHIP?/OBI  
L77 ( 8021) SEA FILE=CAPLUS ABB=ON REPERTOIR?  
L78 ( 1128901) SEA FILE=CAPLUS ABB=ON INTERACT?  
L79 ( 27) SEA FILE=CAPLUS ABB=ON (L74 OR L75 OR L77) AND L76(L) L78  
L80 ( 22) SEA FILE=CAPLUS ABB=ON 9/SC, SX AND L79  
L81 ( 165038) SEA FILE=CAPLUS ABB=ON FIRST AND SECOND  
L82 2 SEA FILE=CAPLUS ABB=ON L80 AND L81

L68 ( 9707) SEA FILE=CAPLUS ABB=ON LIBRARY/CW  
L69 ( 541) SEA FILE=CAPLUS ABB=ON CMBI/RL  
L70 ( 8247) SEA FILE=CAPLUS ABB=ON MICROARRAY?/OBI OR BIOCHIP?/OBI  
L71 ( 8021) SEA FILE=CAPLUS ABB=ON REPERTOIR?  
L72 ( 4201) SEA FILE=CAPLUS ABB=ON JUXTAPOS?  
L73 1 SEA FILE=CAPLUS ABB=ON (L68 OR L69 OR L71) AND L70 AND (L72)

L64 ( 541) SEA FILE=CAPLUS ABB=ON CMBI/RL  
L65 ( 8247) SEA FILE=CAPLUS ABB=ON MICROARRAY?/OBI OR BIOCHIP?/OBI  
L66 ( 141869) SEA FILE=CAPLUS ABB=ON ANTIBODIES/CT  
L67 6 SEA FILE=CAPLUS ABB=ON L66 AND L64 AND L65

L56 ( 9707) SEA FILE=CAPLUS ABB=ON LIBRARY/CW  
L57 ( 541) SEA FILE=CAPLUS ABB=ON CMBI/RL  
L58 ( 266991) SEA FILE=CAPLUS ABB=ON CHANNEL?  
L59 ( 168613) SEA FILE=CAPLUS ABB=ON ETCH?  
L60 ( 8247) SEA FILE=CAPLUS ABB=ON MICROARRAY?/OBI OR BIOCHIP?/OBI  
L61 ( 8021) SEA FILE=CAPLUS ABB=ON REPERTOIR?  
L62 ( 9) SEA FILE=CAPLUS ABB=ON (L56 OR L57 OR L61) AND L60 AND (L58  
OR L59)  
L63 4 SEA FILE=CAPLUS ABB=ON L62 NOT (ION OR CHLORIDE OR ANION) (A) L5  
8

=> s (1107 or 194 or 182 or 173 or 167 or 163) not 155

L166 13 (L107 OR L94 OR L82 OR L73 OR L67 OR L63) NOT (L55)

*previously printed*

=> fil wpids; d que l140; d que l133; d que l126; d que l115

FILE 'WPIDS' ENTERED AT 10:59:16 ON 12 NOV 2002  
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FILE LAST UPDATED: 8 NOV 2002 <20021108/UP>  
MOST RECENT DERWENT UPDATE: 200272 <200272/DW>  
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>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY >>>

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SEE <http://www.derwent.com/dwpi/updates/dwpicov/index.html> <<<

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[http://www.stn-international.de/training\\_center/patents/stn\\_guide.pdf](http://www.stn-international.de/training_center/patents/stn_guide.pdf) <<<

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GUIDES, PLEASE VISIT:  
[http://www.derwent.com/userguides/dwpi\\_guide.html](http://www.derwent.com/userguides/dwpi_guide.html) <<<

L134( 12647)SEA FILE=WPIDS ABB=ON REPERTOIR? OR LIBRAR?  
L135( 2247)SEA FILE=WPIDS ABB=ON MICROARRAY? OR MICRO ARRAY? OR BIOCHIP?  
OR BIO CHIP?  
L136( 124088)SEA FILE=WPIDS ABB=ON ARRAY?  
L137( 11803)SEA FILE=WPIDS ABB=ON HEAVY AND LIGHT  
L138( 51348)SEA FILE=WPIDS ABB=ON ANTIBOD? OR IMMUNOGLOBULIN#  
L139( 9)SEA FILE=WPIDS ABB=ON L134 AND (L135 OR L136) AND L137 AND  
L138  
L140 5 SEA FILE=WPIDS ABB=ON L139 AND (DOMAIN# OR TARGET#)/TI

L127( 12647)SEA FILE=WPIDS ABB=ON REPERTOIR? OR LIBRAR?  
L128( 2247)SEA FILE=WPIDS ABB=ON MICROARRAY? OR MICRO ARRAY? OR BIOCHIP?  
OR BIO CHIP?  
L129( 872571)SEA FILE=WPIDS ABB=ON FIRST AND SECOND  
L130( 118904)SEA FILE=WPIDS ABB=ON INTERACT?  
L131( 124088)SEA FILE=WPIDS ABB=ON ARRAY?  
L132( 64486)SEA FILE=WPIDS ABB=ON INTERSECT?  
L133 3 SEA FILE=WPIDS ABB=ON L127 AND (L128 OR L131) AND (L129 OR  
L130) AND L132 .

L116( 12647)SEA FILE=WPIDS ABB=ON REPERTOIR? OR LIBRAR?  
L117( 2247)SEA FILE=WPIDS ABB=ON MICROARRAY? OR MICRO ARRAY? OR BIOCHIP?  
OR BIO CHIP?  
L118( 872571)SEA FILE=WPIDS ABB=ON FIRST AND SECOND  
L119( 118904)SEA FILE=WPIDS ABB=ON INTERACT?  
L120( 124088)SEA FILE=WPIDS ABB=ON ARRAY?  
L121( 55)SEA FILE=WPIDS ABB=ON L116 AND (L117 OR L120) AND L118 AND  
L119

L122( 384115)SEA FILE=WPIDS ABB=ON S03/DC - Derwent code S03 = Scientific  
L123( 21)SEA FILE=WPIDS ABB=ON L121 AND L122 *instrumentation*  
L124( 110588)SEA FILE=WPIDS ABB=ON ETCH?  
L125( 396013)SEA FILE=WPIDS ABB=ON CHANNEL?  
L126 3 SEA FILE=WPIDS ABB=ON L123 AND (L124 OR L125) \*

L111( 12647)SEA FILE=WPIDS ABB=ON REPERTOIR? OR LIBRAR?  
L112( 2247)SEA FILE=WPIDS ABB=ON MICROARRAY? OR MICRO ARRAY? OR BIOCHIP?  
OR BIO CHIP?  
L113( 12158)SEA FILE=WPIDS ABB=ON JUXTAPOS?  
L114( 124088)SEA FILE=WPIDS ABB=ON ARRAY?  
L115 3 SEA FILE=WPIDS ABB=ON L111 AND (L112 OR L114) AND L113

=> s (l140 or l133 or l126 or l115) not l110

L167 10 (L140 OR L133 OR L126 OR L115) NOT L110

*previously  
printed*

=> fil biosis; d que l162; d que l157; d que l148

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FILE COVERS 1969 TO DATE.  
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT  
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RECORDS LAST ADDED: 7 November 2002 (20021107/ED)

L158( 35392)SEA FILE=BIOSIS ABB=ON MICROARRAY? OR ARRAY? OR BIOCHIP# OR  
BIO CHIP#  
L159( 54364)SEA FILE=BIOSIS ABB=ON LIBRAR? OR REPERTOIRE#  
L160( 131528)SEA FILE=BIOSIS ABB=ON FIRST AND SECOND  
L161( 20)SEA FILE=BIOSIS ABB=ON L158 AND L159 AND L160  
L162 2 SEA FILE=BIOSIS ABB=ON L161 AND (TARGET OR INTERACT?)/TI

L149( 35392)SEA FILE=BIOSIS ABB=ON MICROARRAY? OR ARRAY? OR BIOCHIP# OR  
BIO CHIP#  
L150( 54364)SEA FILE=BIOSIS ABB=ON LIBRAR? OR REPERTOIRE#  
L151( 161001)SEA FILE=BIOSIS ABB=ON CHANNEL?  
L152( 5404)SEA FILE=BIOSIS ABB=ON ETCH?  
L153( 519392)SEA FILE=BIOSIS ABB=ON INTERACT?  
L154( 575964)SEA FILE=BIOSIS ABB=ON LINE# OR TUBE#  
L155( 32)SEA FILE=BIOSIS ABB=ON L149(10A) (L151 OR L152 OR L154) AND  
L150  
L156( 171935)SEA FILE=BIOSIS ABB=ON SCREEN?  
L157 2 SEA FILE=BIOSIS ABB=ON L155 AND L153 AND L156

L144( 35392)SEA FILE=BIOSIS ABB=ON MICROARRAY? OR ARRAY? OR BIOCHIP# OR  
BIO CHIP#  
L145( 54364)SEA FILE=BIOSIS ABB=ON LIBRAR? OR REPERTOIRE#  
L146( 12894)SEA FILE=BIOSIS ABB=ON HEAVY AND LIGHT  
L147( 607934)SEA FILE=BIOSIS ABB=ON ANTIBOD? OR IMMUNOGLOBULIN#  
L148 4 SEA FILE=BIOSIS ABB=ON L146 AND L147 AND L144 AND L145

=> s (l162 or l157 or l148) not l143

L168 8 (L162 OR L157 OR L148) NOT L143

*previously  
printed*

=> dup rem l166,l168,l164,l165,l167

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PROCESSING COMPLETED FOR L166  
PROCESSING COMPLETED FOR L168  
PROCESSING COMPLETED FOR L164  
PROCESSING COMPLETED FOR L165  
PROCESSING COMPLETED FOR L167

L169 41 DUP REM L166 L168 L164 L165 L167 (3 DUPLICATES REMOVED)

ANSWERS '1-13' FROM FILE CAPLUS  
ANSWERS '14-21' FROM FILE BIOSIS  
ANSWERS '22-28' FROM FILE BIOTECHNO  
ANSWERS '29-33' FROM FILE BIOTECHDS  
ANSWERS '34-41' FROM FILE WPIDS

=> d ibib ab 1-41; fil hom

L169 ANSWER 1 OF 41 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1  
ACCESSION NUMBER: 2002:539851 CAPLUS  
DOCUMENT NUMBER: 137:108306  
TITLE: Assembly and screening of highly complex repertoires  
of antibodies or other proteins showing somatic  
variation in yeast  
INVENTOR(S): Zhu, Li; Hua, Shaobing Benjamin; Sheridan, James; Lin,  
Yu-Huei  
PATENT ASSIGNEE(S): Genetastix Corporation, USA  
SOURCE: PCT Int. Appl., 202 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002055718	A2	20020718	WO 2001-US51044	20011031

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,  
UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-703399 A1 20001031

AB Compsn., methods, and kits are provided for efficiently generating and  
screening a library of highly diverse protein complexes for their ability  
to bind to other proteins or oligonucleotide sequences. In one aspect of  
the invention, a library of expression vectors is provided for expressing

the library of protein complexes. The library comprises a first nucleotide sequence encoding a first polypeptide subunit; and a second nucleotide sequence encoding a second polypeptide subunit. The first and second nucleotide sequences each independently varies within the library of expression vectors. In addn., the first and second polypeptide subunit are expressed as sep. proteins which self-assemble to form a protein complex, such as a double-chain antibody fragment (dcFv or Fab) and a fully assembled antibody, in cells into which the library of expression vectors are introduced. The library of expression vectors can be efficiently generated in yeast cells through homologous recombination; and the encoded proteins complexes with high binding affinity to their target mol. can be selected by high throughput screening in vivo or in vitro.

L169 ANSWER 2 OF 41 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2  
 ACCESSION NUMBER: 2002:10544 CAPLUS  
 DOCUMENT NUMBER: 136:84694  
 TITLE: High throughput generation and screening of fully human antibody repertoire in yeast  
 INVENTOR(S): Zhu, Li; Hua, Shaobing Benjamin  
 PATENT ASSIGNEE(S): Genetastix Corporation, USA  
 SOURCE: PCT Int. Appl., 251 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000729	A2	20020103	WO 2001-US20542	20010625
WO 2002000729	A3	20020613		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6406863	B1	20020618	US 2000-603663	20000623
US 6410271	B1	20020625	US 2000-602373	20000623
US 6410246	B1	20020625	US 2000-603658	20000623
PRIORITY APPLN. INFO.:			US 2000-602373	A1 20000623
			US 2000-602972	A 20000623
			US 2000-602973	A1 20000623
			US 2000-603658	A1 20000623
			US 2000-603663	A1 20000623
AB Compns., kits and methods are provided for generating highly diverse libraries of proteins such as antibodies via homologous recombination in vivo, and screening these libraries against protein, peptide and nucleic acid targets using a two-hybrid method in yeast. The method for screening a library of tester fusion proteins against a target protein or peptide comprises: expressing a library of tester proteins in yeast cells, the tester fusion protein comprising a first polypeptide subunit whose sequence varies within the library, a second polypeptide subunit whose sequence varies within the library independently of the first polypeptide, and a linker peptide which links the first and second polypeptide subunits; expressing one or more target fusion proteins in the yeast cells expressing the tester proteins, each of the target fusion proteins comprising a target peptide or protein; and selecting those yeast cells in which a reporter gene is expressed, the expression of the reporter gene being activated by binding of the tester fusion protein to the target				



fusion protein.

L169 ANSWER 3 OF 41 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3  
ACCESSION NUMBER: 2001:694874 CAPLUS  
DOCUMENT NUMBER: 136:242687  
TITLE: Nitrate-induced genes in tomato roots. Array analysis reveals novel genes that may play a role in nitrogen nutrition  
AUTHOR(S): Wang, Yi-Hong; Garvin, David F.; Kochian, Leon V.  
CORPORATE SOURCE: United States Plant, Soil, Laboratory, United States Department of Agriculture-Agricultural Research Service, Cornell University, Ithaca, NY, 14853, USA  
SOURCE: Plant Physiology (2001), 127(1), 345-359  
CODEN: PLPHAY; ISSN: 0032-0889  
PUBLISHER: American Society of Plant Biologists  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB A subtractive tomato (*Lycopersicon esculentum*) root cDNA library enriched in genes up-regulated by changes in plant mineral status was screened with labeled mRNA from roots of both nitrate-induced and mineral nutrient-deficient (-nitrogen [N], -phosphorus, -potassium [K], -sulfur, -magnesium, -calcium, -iron, -zinc, and -copper) tomato plants. A subset of cDNAs was selected from this library based on mineral nutrient-related changes in expression. Addnl. cDNAs were selected from a second mineral-deficient tomato root library based on sequence homol. to known genes. These selection processes yielded a set of 1,280 mineral nutrition-related cDNAs that were arrayed on nylon membranes for further anal. These high-d. arrays were hybridized with mRNA from tomato plants exposed to nitrate at different time points after N was withheld for 48 h, for plants that were grown on nitrate/ammonium for 5 wk prior to the withholding of N. One hundred-fifteen genes were found to be up-regulated by nitrate resupply. Among these genes were several previously identified as nitrate responsive, including nitrate transporters, nitrate and nitrite reductase, and metabolic enzymes such as transaldolase, transketolase, malate dehydrogenase, asparagine synthetase, and histidine decarboxylase. We also identified 14 novel nitrate-inducible genes, including: (a) water **channels**, (b) root phosphate and K<sup>+</sup> transporters, (c) genes potentially involved in transcriptional regulation, (d) stress response genes, and (e) ribosomal protein genes. In addn., both families of nitrate transporters were also found to be inducible by phosphate, K, and iron deficiencies. The identification of these novel nitrate-inducible genes is providing avenues of research that will yield new insights into the mol. basis of plant N nutrition, as well as possible networking between the regulation of N, phosphorus, and K nutrition.  
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L169 ANSWER 4 OF 41 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2002:575356 CAPLUS  
DOCUMENT NUMBER: 137:121886  
TITLE: Microdevices containing photorecognizable coding patterns and methods of using and producing the same thereof  
INVENTOR(S): Wu, Lei; Wang, Xiaobo; Tao, Gouliang; Xu, Junquan; Cheng, Jing; Huang, Mingxiang; Sun, Baoquan; Liu, Litian; Chen, Depu; Rothwarf, David M.; Yang, Weiping  
PATENT ASSIGNEE(S): Aviva Biosciences Corporation, USA  
SOURCE: PCT Int. Appl., 104 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002059603	A2	20020801	WO 2002-US850	20020111
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002137059	A1	20020926	US 2001-924428	20010807
PRIORITY APPLN. INFO.: US 2001-264458P P 20010126				
CN 2001-104318 A 20010228				
US 2001-924428 A 20010807				

AB This invention relates generally to the field of moiety or mol. anal., isolation, detection and manipulation and library synthesis. In particular, the invention provides a microdevice comprises; (a) a substrate; and (b) a photorecognizable coding pattern on said substrate. Preferably, the microdevice does not comprise an anodized metal surface layer. Methods and kits for isolating, detecting and manipulating moieties, and synthesizing libraries using the microdevices are also provided. The invention further provides two-dimensional optical encoders and uses thereof.

L169 ANSWER 5 OF 41 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:293516 CAPLUS

DOCUMENT NUMBER: 136:291317

TITLE: Template platens for the preparation of high density ordered arrays of materials for analytical use

INVENTOR(S): Hess, Robert A.; Kanigan, Tanya S.; Brennan, Colin J. H.; Ozbal, Can; Linton, John Dudley

PATENT ASSIGNEE(S): Biotrove, Inc., USA

SOURCE: PCT Int. Appl., 135 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030561	A2	20020418	WO 2001-US31770	20011010
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002094533	A1	20020718	US 2001-975496	20011010
PRIORITY APPLN. INFO.: US 2000-239538P P 20001010				
US 2001-268894P P 20010214				
US 2001-284710P P 20010418				

AB The invention features methods of making devices, or "platens" having a high-d. array of through-holes, as well as methods of cleaning and refurbishing the surfaces of the platens. The invention further features methods of making high-d. arrays of chem., biochem., and biol. compds., having many advantages over conventional, lower-d. arrays. The invention

includes methods by which many phys., chem. or biol. transformations can be implemented in serial or in parallel within each addressable through-hole of the devices. Addnl., the invention includes methods of analyzing the contents of the array, including assaying of phys. properties of the samples. In various embodiments, the reagents can be contained within the through-holes by capillary action, attached to the walls of the through-hole. The porous material can be, for example, a gel, a bead, sintered glass, or particulate matter, or can be the inner wall of a through-hole that has been chem. **etched**. In particular embodiments, the arrays can include individual mols., complexes of mols., viruses, cells, groups of cells, pieces of tissue, or small particles or beads. The members of the arrays can also, for example, function as transducers that report the presence of an analyte (e.g., by providing an easily detected signal), or they can function as selective binding agents for the retention of analytes of interest. Using these methods, arrays corresponding to a large plurality of human genes (e.g., using nucleic acid probes) can also be prepd.

L169 ANSWER 6 OF 41 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:716938 CAPLUS  
DOCUMENT NUMBER: 137:244249  
TITLE: Non-specific binding resistant protein arrays and methods for making the same  
INVENTOR(S): Wagner, Peter; Kern, Peter; Lu, Hongbo; Tran, Huu  
PATENT ASSIGNEE(S): USA  
SOURCE: U.S. Pat. Appl. Publ., 36 pp., Cont.-in-part of U.S. 6,329,209.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 7  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002132272	A1	20020919	US 2001-46442	20011027
US 6406921	B1	20020618	US 1998-115455	19980714
US 6329209	B1	20011211	US 1999-353555	19990714
PRIORITY APPLN. INFO.:			US 1998-115455 A2	19980714
			US 1999-353555 A2	19990714

AB Arrays of protein-capture agents useful for the simultaneous detection of a plurality of proteins which are the expression products, or fragments thereof, of a cell or population of cells in an organism are provided. A variety of antibody arrays, in particular, are described. Methods of both making and using the arrays of protein-capture agents are also disclosed. The invention arrays are particularly useful for various proteomics applications including assessing patterns of protein expression and modification in cells.

L169 ANSWER 7 OF 41 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:429481 CAPLUS  
DOCUMENT NUMBER: 137:2759  
TITLE: Linker and method for solid phase combinatorial library screening  
INVENTOR(S): Coffen, David L.; Pigliucci, Riccardo; Xiao, Xiao-yi  
PATENT ASSIGNEE(S): USA  
SOURCE: U.S. Pat. Appl. Publ., 16 pp.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002068367	A1	20020606	US 2001-975137	20011010

PRIORITY APPLN. INFO.: US 2000-239564P P 20001011

AB A high throughput screening method for detecting interactions between proteins, nucleic acids and small mols. comprises coating a solid support surface with a substance, such as streptavidin, that has a high affinity for a ligand, such as biotin, that may be readily attached to a library of compds. via a linker mol. The biotin linked library members are spotted onto the streptavidin in a pattern and screened for binding to other compds. of interest. Thus, it is possible to screen much smaller quantities of compds. than would be possible in a multiwell format. Due to the high affinity of biotin for streptavidin, there is no diffusion of the compds. on the solid support. Moreover, the method provides a high throughput, low cost screen that may be accomplished completely manually without the use of expensive fluid handling robots.

L169 ANSWER 8 OF 41 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:519203 CAPLUS  
DOCUMENT NUMBER: 137:165753  
TITLE: Isolation of receptor-ligand pairs by capture of long-lived multivalent interaction complexes  
AUTHOR(S): De Wildt, Ruud M. T.; Tomlinson, Ian M.; Ong, Jennifer L.; Holliger, Philipp  
CORPORATE SOURCE: Medical Research Council Laboratory of Molecular Biology, Cambridge, CB2 2QH, UK  
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2002), 99(13), 8530-8535  
CODEN: PNASA6; ISSN: 0027-8424  
PUBLISHER: National Academy of Sciences  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB We have combined phage display and array screening for the rapid isolation of pairs of interacting polypeptides. Our strategy, named SAC (selection by avidity capture), is based on the avidity effect, the formation of highly stable complexes formed by multivalent interactions; in our case, between a receptor (multivalently displayed on phage) and a ligand (coexpressed as a multimeric fusion protein). Capture of the long-lived interaction complex allows the isolation of phage bearing cognate interaction pairs, as we demonstrate for a range of interactions, including Ab-antigen pairs and the rapamycin-dependent interaction of FKBP-12 and FRAP. Cognate phage are enriched by SAC up to 1000-fold and interacting pairs can be identified by array screening. Application of SAC to Ab-antigen interactions as a model system yielded over 140 specific Abs to a single antigen and 92 Abs to three different fetal human brain antigens in a single round of SAC each. Our results suggest that SAC should prove useful for the identification and study of receptor-ligand interactions in particular among extracellular proteins, as well as for the rapid generation of specific Abs to **multiple** antigens.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L169 ANSWER 9 OF 41 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:745746 CAPLUS  
TITLE: Oligosaccharide **microarrays** for high-throughput detection and specificity assignments of carbohydrate-protein **interactions**  
AUTHOR(S): Fukui, Shigeyuki; Feizi, Ten; Galustian, Christine; Lawson, Alexander M.; Chai, Wengang  
CORPORATE SOURCE: Imperial College Faculty of Medicine, Glycosciences Laboratory, Northwick Park Hospital, Middlesex, HA1 3UJ, UK  
SOURCE: Nature Biotechnology (2002), 20(10), 1011-1017

CODEN: NABIF9; ISSN: 1087-0156  
PUBLISHER: Nature Publishing Group  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB We describe microarrays of oligosaccharides as neoglycolipids and their robust display on nitrocellulose. The arrays are sourced from glycoproteins, glycolipids, proteoglycans, polysaccharides, whole organs, or from chem. synthesized oligosaccharides. We show that carbohydrate-recognizing proteins single out their ligands not only in arrays of homogeneous oligosaccharides but also in arrays of heterogeneous oligosaccharides. Initial applications have revealed new findings, including: (i) among O-glycans in brain, a relative abundance of the Lewis<sup>x</sup> sequence based on N-acetyllactosamine recognized by anti-L5, and a paucity of the Lewis<sup>x</sup> sequence based on poly-N-acetyllactosamine recognized by anti-SSEA-1; (ii) insights into chondroitin sulfate oligosaccharides recognized by an antiserum and an antibody (CS-56) to chondroitin sulfates; and (iii) binding of the cytokine interferon- $\gamma$  (IFN- $\gamma$ ) and the chemokine RANTES to sulfated sequences such as HNK-1, sulfo-Lewis<sup>x</sup>, and sulfo-Lewis<sup>a</sup>, in addn. to glycosaminoglycans. The approach opens the way for discovering new carbohydrate-recognizing proteins in the proteome and for mapping the repertoire of carbohydrate recognition structures in the glycome.

REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L169 ANSWER 10 OF 41 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:781183 CAPLUS

DOCUMENT NUMBER: 135:328960

TITLE: Library screening system to detect protein-protein interactions

INVENTOR(S): Lilien, Jack; Elferink, Lisa A.; Balsamo, Janne; Kamholz, John

PATENT ASSIGNEE(S): Wayne State University, USA

SOURCE: PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001079559	A1	20011025	WO 2001-US12457	20010418
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 2002081570	A1	20020627	US 2001-836865	20010418

PRIORITY APPLN. INFO.: US 2000-198122P P 20000418

AB The invention concerns a method for screening protein-protein interactions that is rapid, easy and generally applicable to a wide array of such interactions is disclosed. This method, an adaptation and combination of certain existing approaches, uses T7 phage display libraries and target epitope arrays synthesized, for example, by simultaneous synthesis overlapping peptides of known sequences. These methods provide for high throughput screening that can identify the particular amino acids or domains or epitopes that are of primary importance in the binding

interactions between **two** protein partners.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L169 ANSWER 11 OF 41 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:137109 CAPLUS

DOCUMENT NUMBER: 134:159850

TITLE: Microfluidic devices for the controlled manipulation  
of small volumes

INVENTOR(S): Ramsey, J. Michael; Jacobson, Stephen C.

PATENT ASSIGNEE(S): UT-Battelle, LLC, USA

SOURCE: PCT Int. Appl., 39 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012327	A1	20010222	WO 2000-US40620	20000810
W:				
AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				
CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,				
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,				
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,				
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,				
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,				
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,				
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1202802	A1	20020508	EP 2000-967377	20000810
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
IE, SI, LT, LV, FI, RO, MK, CY, AL				
PRIORITY APPLN. INFO.:			US 1999-148502P	P 19990812
			US 1999-408060	A1 19990929
			WO 2000-US40620	W 20000810

AB A method for conducting a broad range of biochem. analyses or manipulations on a series of nano- to subnanoliter reaction vols. and an app. for carrying out the same are disclosed. The method and app. are implemented on a fluidic microchip to provide high serial throughput. The method and device of the invention also lend themselves to multiple parallel analyses and manipulation to provide greater throughput for the generation of biochem. information. In particular, the disclosed device is a microfabricated **channel** device that can manipulate nanoliter or subnanoliter biochem. reaction vols. in a controlled manner to produce results at rates of 1 to 10 Hz per **channel**. The individual reaction vols. are manipulated in serial fashion analogous to a digital shift register. The method and app. according to this invention have application to such problems as screening mol. or cellular targets using single beads from split-synthesis combinatorial libraries, screening single cells for RNA or protein expression, genetic diagnostic screening at the single cell level, or performing single cell signal transduction studies.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L169 ANSWER 12 OF 41 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:813298 CAPLUS

DOCUMENT NUMBER: 135:341133

TITLE: Compact disk sample carrier for high throughput  
screening associated with **two**-dimensional  
reflectometric detection of molecular interactions

PATENT ASSIGNEE(S): Institut fuer Physikalische Hochtechnologie e.V.,

SOURCE: Germany; Fritzsche, Wolfgang  
Ger. Gebrauchsmusterschrift, 10 pp.  
CODEN: GGXXFR  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 20111022	U1	20011108	DE 2001-20111022	20010629

PRIORITY APPLN. INFO.: DE 2000-10033360 A1 20000701

AB The invention concerns a compact disk (CD) support for high throughput screening of mol. interactions that contains tracks with immobilized std. spots and specific binding spots; upon contacting the disk with the sample soln. the target mols. bind to the disk; the bound mols. are labeled with light scattering substances; the disk is scanned for reflected light and the spots are identified with the help of the std. spots. Thus 969 oligonucleotide probes were immobilized onto a mini CD; after contacting the disk with DNA sample, the disk was rinsed to remove the non-specifically bound DNA; the disk with the hybridized DNA was treated with a colloid suspension contg. gold particles bound to oligonucleotides that were specific for the bound oligos but not specific for the binding spots. The second hybridization resulted 110 particles/.mu.m2. The device can be used for combinatorial libraries too.

L169 ANSWER 13 OF 41 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:719627 CAPLUS  
DOCUMENT NUMBER: 128:951  
TITLE: Method of identifying sequence in a nucleic acid target using interactive sequencing by hybridization with applications of combinatorial algorithm  
INVENTOR(S): Skiena, Steven S.  
PATENT ASSIGNEE(S): Biota Corp., USA  
SOURCE: U.S., 12 pp.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5683881	A	19971104	US 1995-546423	19951020

AB A new approach is proposed for sequencing by hybridization (SBH), which uses interaction to dramatically reduce the no. of oligonucleotides used for de novo sequencing of large DNA fragments, while preserving the parallelism which is the primary advantage of SBH. In particular, a series of rounds is performed, starting from an initial fixed oligonucleotide array, of hybridizing a target sample against an array, and then designing a new oligonucleotide array/customized sequencing biochip in response to the results of the rounds to date, until the sequence is detd. This method offers the potentials of higher throughput and reduced cost. In addn., crit. techniques which capture the combinatorial advantages of interaction to minimize the size of arrays needed for sequencing large DNA fragments, while preserving parallelism and minimizing the no. of exptl. rounds needed for sequencing.

L169 ANSWER 14 OF 41 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:539336 BIOSIS  
DOCUMENT NUMBER: PREV200100539336  
TITLE: Characterization of the DISC1 protein.  
AUTHOR(S): Morris, J. A. (1); Ma, L. (1); Kandpal, G. (1); Bruce, J.

E.; Tang, X.; Lu, M. (1); Acton, P.; Gerhold, D. (1); Austin, C. P. (1)  
CORPORATE SOURCE: (1) Pharmacology, Merck and Co., West Point, PA USA  
SOURCE: Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 1493. print.  
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001  
ISSN: 0190-5295.  
DOCUMENT TYPE: Conference  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB DISC1 (Disrupted-In-Schizophrenia 1) is a candidate gene for schizophrenia. A translocation between chromosomes 1 and 11 which resulted in interruption of DISC1 segregated with schizophrenia in a Scottish family. We have been examining the expression and potential function of the full-length DISC1 protein along with the DISC1 protein truncated at the translocation breakpoint. SH-SY5Y cells were stably transfected with C-terminal tagged full-length and truncated DISC1 cDNAs. Western analysis verified over-expression. Immunohistochemical analysis is being done to determine protein localization. Expression studies are also being completed on the over-expressing cell lines by **microarray** analysis. Protein-protein **interactions** are being examined by yeast two hybrid analysis. Using DISC1 as a bait, we have **screened** human expression **libraries** and have found positive **interactions**. We are verifying these **interactions** and identifying the proteins. Proteomics experiments are underway to verify DISC1 antibody specificity essential to the protein localization studies, identify other proteins that co-immunoprecipitate with DISC1, and validate the identities of **interacting** gene products found in the yeast two hybrid system. In addition, protein profiling experiments are being performed using differential 2D isoelectric gel electrophoresis to highlight those proteins with expression patterns that are modulated with DISC1 expression. These studies will identify proteins that **interact** with DISC1, the pathways involving this gene product, and provide information relevant to the function of the DISC1 protein and its potential role in schizophrenia.

L169 ANSWER 15 OF 41 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:222902 BIOSIS

DOCUMENT NUMBER: PREV200200222902

TITLE: PCR generation of highly specific 16S rRNA-targeted oligonucleotide probes without prior knowledge of the **target** sequence.

AUTHOR(S): Bertilsson, S. (1); Cavanaugh, C. M.; Polz, M. F. (1)

CORPORATE SOURCE: (1) Massachusetts Institute of Technology, Cambridge, MA USA

SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (2001) Vol. 101, pp. 501.  
<http://www.asmta.org/mtgsrsrc/generalmeeting.htm>. print.  
Meeting Info.: 101st General Meeting of the American Society for Microbiology Orlando, FL, USA May 20-24, 2001  
ISSN: 1060-2011.

DOCUMENT TYPE: Conference

LANGUAGE: English

AB Specific oligonucleotide probes targeting the small subunit rRNA are commonly used to detect and quantify bacteria in natural environments. We developed a PCR-based approach that allows synthesis of population-specific bacterial oligonucleotide probes targeting the 16S rRNA without the need for either sequencing or isolation of the target organisms. The procedure is based on a two-step PCR amplification of a variable region in the 16S rDNA using 3 universal bacterial primers. In the **first** amplification, a double stranded product is generated



followed by a single stranded amplification. From both products, the primers are detached after each amplification ultimately leaving a single stranded hypervariable sequence stretch of about 30 bp. A major advantage of the method is that labeled nucleotides can be incorporated during the **second** amplification yielding high activity probes. We used a model system consisting of 25 closely and distantly related bacterial strains isolated from coastal water to test the specificity and hybridization behavior of these PCR-generated probes. As demonstrated in the accompanying poster, this method will be most useful for the rapid and economical generation of oligonucleotide **arrays** from clone **libraries** of environmental microorganisms to determine the abundance and activity patterns of microbial populations.

L169 ANSWER 16 OF 41 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1999:325870 BIOSIS

DOCUMENT NUMBER: PREV199900325870

TITLE: Making artificial **antibodies**: A format for phage display of combinatorial heterodimeric **arrays**.

AUTHOR(S): Gao, Changshou; Mao, Shenlan; Lo, Chih-Hung L.; Wirsching, Peter; Lerner, Richard A. (1); Janda, Kim D. (1)

CORPORATE SOURCE: (1) Departments of Chemistry and Molecular Biology, Scripps Research Institute and Skaggs Institute for Chemical Biology, 10550 North Torrey Pines Road, La Jolla, CA, 92037 USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (May 25, 1999) Vol. 96, No. 11, pp. 6025-6030.  
ISSN: 0027-8424.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The gene VII protein (pVII) and gene IX protein (pIX) are associated closely on the surface of filamentous bacteriophage that is opposite of the end harboring the widely exploited pIII protein. We developed a phagemid format wherein **antibody heavy-** and **light-chain** variable regions were fused to the amino termini of pVII and pIX, respectively. Significantly, the fusion proteins interacted to form a functional Fv-binding domain on the phage surface. Our approach will be applicable to the display of generic peptide and protein **libraries** that can form combinatorial heterodimeric **arrays**. Consequently, it represents a first step toward artificial **antibodies** and the selection of novel biological activities.

L169 ANSWER 17 OF 41 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1997:167650 BIOSIS

DOCUMENT NUMBER: PREV199799474253

TITLE: Gene structure, promoter activity, and chromosomal location of the DR-nm23 gene, a related member of the nm23 gene family.

AUTHOR(S): Martinez, Robert; Venturelli, Donatella; Perrotti, Danilo; Veronese, Maria Luisa; Kastury, Kumar; Druck, Teresa; Huebner, Kay; Calabretta, Bruno (1)

CORPORATE SOURCE: (1) Dep. Microbiol. Immunol., Kimmel Cancer Inst., Blueemle Life Sci. Build., Thomas Jefferson Univ., 233 South 10th St., Room 630, Philadelphia, PA 19107 USA

SOURCE: Cancer Research, (1997) Vol. 57, No. 6, pp. 1180-1187.  
ISSN: 0008-5472.

DOCUMENT TYPE: Article

LANGUAGE: English

AB DR-nm23 cDNA was cloned recently by differential **screening** of a cDNA **library** derived from chronic myelogenous leukemia-blast crisis primary cells. It is highly homologous to the putative metastasis suppressor nm23-H1 gene and the closely related nm23-H2 gene. When

overexpressed in the myeloid precursor 32Dcl3 cell line, it inhibited granulocyte colony-stimulating factor-stimulated granulocytic differentiation and induced apoptosis. We have now found that the expression of DR-nm23 is not restricted to hematopoietic cells but is also detected in an **array** of solid tumor cell **lines**, including carcinoma of the breast, colon, and prostate, as well as the glioblastoma cell line T98G. We have also isolated both the gene and its 5'-flanking region and found that DR-nm23 localizes on chromosome 16q13. The gene consists of six exons and five introns. When fused in-frame to the nucleotide sequence for the green fluorescent protein and transfected in SAOS-2 cells, it generates a protein of the predicted size that localizes to the cytoplasm. The 5'-flanking region of DR-nm23 does not contain a canonical TATA box or a CAAT box, but it is G+C rich and contains two binding sites for the developmentally regulated transcription factor activator protein 2 (AP-2). Transient expression assays of DR-nm23 promoter-chloramphenicol acetyltransferase constructs demonstrated that the segment from nucleotides -1028 to +123 has the highest activity in hematopoietic K562 cells and in TK-ts13 hamster fibroblasts. Moreover, AP-2 induced a 3-fold transactivation of the DR-nm23 5'-flanking segment from nucleotides -1676 to +123 and **interacted** specifically with oligomers containing putative AP-2 binding sites (-936 to -909, and -548 to -519) as indicated by electrophoretic mobility shift assay. Furthermore, nuclear run-on assays from high and low DR-nm23-expressing cells (K562 and CCRF-CEM, respectively) revealed similar transcription rates. Therefore, the regulation of the DR-nm23 gene expression might involve other mechanisms occurring at posttranscriptional and/or translational levels.

L169 ANSWER 18 OF 41 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1995:298980 BIOSIS

DOCUMENT NUMBER: PREV199598313280

TITLE: Characterisation of epitopes on human p53 using phage-displayed peptide **libraries**: Insights into antibody-peptide **interactions**.

AUTHOR(S): Stephen, Charles W.; Helminen, Paivi; Lane, David P.

CORPORATE SOURCE: CRC Cell Transformation Res. Group, CRC Lab., Dep. Biochem., Univ. Dundee, Dundee DD1 4HN UK

SOURCE: Journal of Molecular Biology, (1995) Vol. 248, No. 1, pp. 58-78.

ISSN: 0022-2836.

DOCUMENT TYPE: Article

LANGUAGE: English

AB We previously described the use of a phage-displayed **library** of random hexapeptides to define and localise the epitope on the human tumor suppressor protein p53 recognised by the monoclonal antibody PAb240. Here we have extended these results to a further eight anti-p53 monoclonal antibodies and to two further **libraries**, which display 12-mer and 20-mer peptides, respectively. **First**, we showed that selection of PAb240 binding clones from the 12-mer and 20-mer **libraries** gives essentially identical results to those obtained by screening the 6-mer **library**. **Second**, we used the 6-mer and 12-mer **libraries** to define the detailed specificity profiles of six antibodies (DO-1, DO-2, DO-7, Bp53-11, Bp53-12 and Bp53-19), which recognise the same short, highly immunogenic N-terminal segment of p53. Finally, we employed all three **libraries** to reveal the distinct mechanisms by which PAb421 and PAb122, two monoclonal antibodies that allosterically activate sequence-specific DNA binding by p53, react specifically with the same positively-charged C-terminal segment. In each case the epitope locations inferred from the selected sequences were confirmed by probing an **array** of overlapping synthetic peptides representing the primary sequence of p53. The results emphasise the consequences for epitope mapping of screening random, as opposed to antigen-derived, peptide **libraries**; specifically (1) that

comparison of selected sequences reveals the contribution of individual residues to binding energy and specificity; (2) that heteroclitic reactions can lead to definition of a consensus that is related to but distinct from the immunising epitope and (3) that isolation of non-immunogen-homologous "mimotope" sequences reveals discrete, alternative ligand structures. The results with PAb421 and PAb122 provide examples where, while selection from the 12-mer and 20-mer **libraries** leads to isolation of immunogen-homologous sequences, selection from the 6-mer **library** results in the isolation either of no binding clones (PAb122) or solely of "mimotope" sequences with no discernible homology to the original antigen (PAb421). In addition the results with PAb421 reveal that linear epitopes can be longer than previously thought and can be formally discontinuous, consisting of independent contact motifs, which show promiscuous relative positioning.

L169 ANSWER 19 OF 41 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1994:211328 BIOSIS

DOCUMENT NUMBER: PREV199497224328

TITLE: Nucleotide sequence analysis of natural and combinatorial anti-PDC-E2 **antibodies** in patients with primary biliary cirrhosis: Recapitulating immune selection with molecular biology.

AUTHOR(S): Pascual, Virginia; Cha, Sanghoon; Gershwin, M. Eric; Capra, J. Donald; Leung, Patrick S. C. (1)

CORPORATE SOURCE: (1) Div. Rheumatology, Allergy Clinical Immunology, TB192-Sch. Med., Univ. Calif., Davis, CA 95616 USA

SOURCE: Journal of Immunology, (1994) Vol. 152, No. 5, pp. 2577-2585.

ISSN: 0022-1767.

DOCUMENT TYPE: Article

LANGUAGE: English

AB We have analyzed at the nucleotide level the variable region gene sequences of five human mAbs and five recombinant Fab fragments derived from the mesenteric lymph nodes of patients with primary biliary cirrhosis. Both mAbs and Fabs were monospecific for dihydrolipoamide acetyltransferase, the E2 subunit of the pyruvate dehydrogenase complex, which has been shown to be the major autoantigen of primary biliary cirrhosis. We found that although the mAbs, mainly of the IgM isotype, were encoded by a diverse **array** of V-H and V-L gene segments either as direct copies of germline genes or somatically mutated, the recombinant IgG Fabs expressed clonally related **heavy** chains displaying a high number of somatic mutations that very likely occurred in the context of Ag selection. Combinatorial pairing of clonally related **heavy** chains with highly homologous **light** chains suggests that the IgG anti-pyruvate dehydrogenase complex **repertoire** of primary biliary cirrhosis patients is the result of the clonal expansion of a restricted set of B cells.

L169 ANSWER 20 OF 41 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1993:183028 BIOSIS

DOCUMENT NUMBER: PREV199395093478

TITLE: What is the selective pressure that maintains the gene loci encoding the antigen receptors of T and B cells? A hypothesis.

AUTHOR(S): Langman, Rodney E. (1); Cohn, Melvin

CORPORATE SOURCE: (1) Developmental Biol., Lab., Salk Inst., PO Box 85800, San Diego, CA 92138-9216

SOURCE: Immunology and Cell Biology, (1992) Vol. 70, No. 6, pp. 397-404.

ISSN: 0818-9641.

DOCUMENT TYPE: Article

LANGUAGE: English

AB The dominant view is that the gene loci encoding the B cell antigen

receptor (BAr) or the T cell antigen receptor (TAr) specify a vast **array** of combining sites. The 'germline' **repertoire** is estimated to be  $10^{10}$  by multiplying numbers of subunit complements by DN-region variability. This implies that the germline can be maintained by a selection imposed by all or most of the antigenic universe. Its unchallenged popularity, notwithstanding, this neo-germline view is untenable and hence the need for a competing concept, as presented here. The **immunoglobulin** (Ig) loci are under a totally different selection from the T loci. The Ig loci are selected upon largely by carbohydrate determinants on pathogens that vary more slowly than the proteins produced by the Ig loci, which are necessary to rid these selective antigens. By contrast, the T loci are selected to recognize the allele-specific determinants on restricting elements encoded in the major histocompatibility complex (MHC). The expression of the germline results in a high copy number (HCN) **repertoire**; this **repertoire** is the substrate for 'mutation' that yields the low copy number (LCN) **repertoire**. For the B cell, these two **repertoires** interact to optimize the response to the unexpected. For the T cell, only the LCN **repertoire** is functional. The **immunoglobulin** (Ig) loci are selected upon as **light**(L)-**heavy** (H) pairs; the T loci are selected upon as single units alpha or beta (i.e. the V-T-gene segments act as a single pool). This competing concept carries with it many important and testable consequences.

L169 ANSWER 21 OF 41 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1989:427252 BIOSIS

DOCUMENT NUMBER: BA88:85510

TITLE: CLONING OF THE IMMUNOLOGICAL **REPertoire** IN  
ESCHERICHIA-COLI FOR GENERATION OF MONOCLONAL CATALYTIC  
**ANTIBODIES** CONSTRUCTION OF A **HEAVY** CHAIN  
VARIABLE REGION-SPECIFIC COMPLEMENTARY DNA **LIBRARY**

AUTHOR(S): SASTRY L; ALTING-MEES M; HUSE W D; SHORT J M; SORGE J A;  
HAY B N; JANDA K D; BENKOVIC S J; LERNER R A

CORPORATE SOURCE: DEP. MOLECULAR BIOL., RES. INST. SCRIPPS CLINIC, 10666  
NORTH TORREY PINES ROAD, LA JOLLA, CALIF. 92037.

SOURCE: PROC NATL ACAD SCI U S A, (1989) 86 (15), 5728-5732.  
CODEN: PNASA6. ISSN: 0027-8424.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB Efficient generation of catalytic **antibodies** is uniquely dependent on the exact nature of the binding interactions in the antigen-**antibody** complex. Current methods for generation of monoclonal **antibodies** do not efficiently survey the immunological **repertoire** and, therefore, they limit the number of catalysts that can be obtained. We are exploring methods to clone and express the immunological **repertoire** in Escherichia coli. As the essential first step, we present here a method for the establishment of a highly diverse **heavy** chain variable region **library**. Consequently, it should now be possible to express and recombine the **heavy** and **light** chain variable region fragments to generate a large **array** of functional combining portions of the **antibody** molecule. This technology may provide an alternative to the hybridoma methodology for accessing the monoclonal **antibody** specificity of the immune system.

L169 ANSWER 22 OF 41 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.

ACCESSION NUMBER: 2002:34680875 BIOTECHNO

TITLE: Differential display: Analysis of gene expression  
during plant cell separation processes

AUTHOR: Whitelaw C.A.; Ruperti B.; Roberts J.A.

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9712 Medical Center Drive, Rockville, MD 20850, United

States.  
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SOURCE: Applied Biochemistry and Biotechnology - Part B  
Molecular Biotechnology, (2002), 21/3 (251-258), 5  
reference(s)  
CODEN: MLBOEO ISSN: 1073-6085  
DOCUMENT TYPE: Journal; Article  
COUNTRY: United States  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB An essential component in the study of cell growth and development in any organism is the analysis of differential gene expression. There are numerous techniques available for comparison of **two** or **more** systems at the molecular level, including subtractive hybridization, reverse transcriptase (RT), polymerase chain reaction (PCR), differential screening of cDNA **libraries**, and, more recently, cDNA **microarrays**. Differential display has advantages in that it is relatively less time-consuming and can result in the identification of rare cDNA, which may be missed by conventional cDNA **library** screening. In addition, cDNA **microarrays** are a valuable asset to the analysis of regulated gene expression but the technique is expensive to employ. Although we successfully applied differential display to isolate novel mRNAs that are up- and downregulated during cell separation processes in plants, the technique can be applied to any system where **two** or **more** mRNA sets are to be compared.

L169 ANSWER 23 OF 41 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.  
ACCESSION NUMBER: 2000:30782569 BIOTECHNO  
TITLE: Identification of differentially expressed genes in the visual structures of brain using high-density cDNA **grids**  
AUTHOR: Prasad S.S.; Kojic L.Z.; Lee S.-S.; Chaudhuri A.; Hetherington P.; Cynader M.S.  
CORPORATE SOURCE: S.S. Prasad, Department of Ophthalmology, University of British Columbia, 2550 Willow Street, Vancouver, BC V5Z 3N9, Canada.  
E-mail: shprasad@home.com  
SOURCE: Molecular Brain Research, (20 OCT 2000), 82/1-2 (11-24), 39 reference(s)  
CODEN: MBREE4 ISSN: 0169-328X  
PUBLISHER ITEM IDENT.: S0169328X00001728  
DOCUMENT TYPE: Journal; Article  
COUNTRY: Netherlands  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB The hybridization patterns of 18,371 high-density-**grid-arrayed** non-redundant complementary DNA (cDNA) clones were examined using three different sources of cDNA probes. The **first** set of probes was synthesized from mRNA isolated from visual brain areas MT and V4 of Vervet monkey. The **second** set of probes was derived from cDNA **libraries** constructed from two micro dissected sets of layers of the monkey Lateral Geniculate Nucleus layers within the visual pathway, namely the magnocellular and parvocellular layers. The third set of cDNA probes was synthesized from the subtracted fractions of the cDNAs enriched for either the magnocellular or the parvocellular layers of the Lateral Geniculate Nucleus. Software, linked directly to the Genbank database, was developed to aid in the rapid identification of both expressed and differentially expressed genes. Our results indicate that both the cDNA probes synthesized from mRNA and cDNA **libraries** can identify similar fractions of expressed genes. However, the subtracted cDNA probes improve the efficiency of detection for those genes that are expressed at much lower abundance. Analyses of

these results for the differential expression patterns of these genes were validated by semi-quantitative PCR on the DNA derived from the whole tissue cDNA **libraries**. A list of some known genes that are statistically differentially expressed within the magnocellular layers of the LGN and area MT in the primate visual areas is derived. (C) 2000 Elsevier Science B.V.

L169 ANSWER 24 OF 41 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.  
ACCESSION NUMBER: 1997:27432596 BIOTECHNO  
TITLE: Cloning and characterization of the Arabidopsis thaliana SQS1 gene encoding squalene synthase involvement of the C-terminal region of the enzyme in the **channeling** of squalene through the sterol pathway  
AUTHOR: Kribii R.; Arro M.; Del Arco A.; Gonzalez V.; Balcells L.; Delourme D.; Ferrer A.; Karst F.; Boronat A.  
CORPORATE SOURCE: A. Boronat, Dept. Bioquímica/Biología Molecular, Facultat de Química, Universitat de Barcelona, Martí Franques 1, E-08028 Barcelona, Spain.  
E-mail: aboronat@sun.bq.ub.es  
SOURCE: European Journal of Biochemistry, (1997), 249/1 (61-69), 38 reference(s)  
CODEN: EJBCAI ISSN: 0014-2956  
DOCUMENT TYPE: Journal; Article  
COUNTRY: Germany, Federal Republic of  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
AB Squalene synthase (SQS) catalyzes the first committed step of the sterol biosynthetic pathway. A full-length Arabidopsis thaliana SQS cDNA has been isolated by combining **library** screening and PCR-based approaches. Arabidopsis SQS is encoded by a small gene family of two genes (SQS1 and SQS2) which are organized in a tandem **array**. SQS1 and SQS2 have an identical organization with regard to intron positions and exon sizes and encode SQS isoforms showing a high level of sequence conservation (79% identity and 88% similarity). The isolated cDNA has been assigned to the SQS1 gene product, SQS1. RNA blot analysis has shown that the 1.6-kb SQS1 mRNA is detected in all plant tissues analyzed (inflorescences, leaves, stems and roots) although the transcript is especially abundant in roots. Arabidopsis SQS1 isoform is unable to complement the SQS-defective Saccharomyces cerevisiae strain 5302, although SQS activity was detected in the microsomal fraction of the transformed yeast strain. However, a chimeric SQS resulting from the replacement of the 66 C-terminal residues of the Arabidopsis enzyme by the 111 C-terminal residues of the Schizosaccharomyces pombe enzyme was able to confer ergosterol prototrophy to strain 5302. Labeling studies using .cents..sup.3H!farnesyl-P.sub.2 and microsomal fractions obtained from yeast strains expressing either Arabidopsis SQS1 or chimeric Arabidopsis/S. pombe SQS derivatives indicated that the C-terminal region of the enzyme is involved in the **channeling** of squalene through the yeast sterol pathway.

L169 ANSWER 25 OF 41 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.  
ACCESSION NUMBER: 1997:27154393 BIOTECHNO  
TITLE: Nucleoside transport inhibitors: Structure-activity relationships and potential therapeutic applications  
AUTHOR: Buolamwini J.K.  
CORPORATE SOURCE: J.K. Buolamwini, Department of Medicinal Chemistry, Res Inst. Pharmaceutical Sciences, University of Mississippi, University, MS 38677, United States.  
SOURCE: Current Medicinal Chemistry, (1997), 4/1 (35-66), 305 reference(s)  
CODEN: CMCHE7 ISSN: 0929-8673  
DOCUMENT TYPE: Journal; General Review

COUNTRY: Netherlands  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB A survey of structure-activity relationships and potential therapeutic applications of nucleoside transport inhibitors is presented. Among the two equilibrative (facilitated diffusion), and five concentrative (sodium-dependent) nucleoside transporters identified in mammalian cells, only the equilibrative transporters (es and ei and one concentrative transporter (cs) can be effectively blocked by one or more of the nucleoside transport inhibitors discovered to date. A structurally diverse **array** of compounds have been shown to exert nucleoside transport inhibitory activity to varying degrees. The most important of these are i) nucleoside analogs of which S.sup.6-(4-nitrobenzyl)mercaptapurine riboside (NBMPR, nitrobenzylthioinosine) is the prototype, ii) pyrimidopyrimidine and pteridine derivatives of which dipyridamole (Persantine) is the prototype, and iii) alkyl- and cycloalkyldiamine and piperazine calcium **channel** antagonists of which dilazep and lidoflazine are the representatives, respectively. All of these are effective inhibitors of the es transporter, but dipyridamole is also a potent inhibitor of the ei transporter with variable activity depending on the cell type. Surprisingly, NBMPR and dipyridamole are also potent inhibitors of the newly identified cs concentrative transporter in fresh leukemia cells from patients. Not only does the es inhibitory potency of these compounds depend on tissue type, but it also varies widely among different mammalian species. Nucleoside transport inhibitors have potential for therapeutic uses in 1) adenosine potentiation in cardioprotection and cerebroprotection in ischemic heart disease and stroke, respectively, 2) the modulation of the effects of antimetabolite anticancer and antiviral agents, and 3) host tissue protection in chemotherapy with cytotoxic nucleosides. Additional areas of potential therapeutic application of NT inhibitors include kidney transplantation, analgesia and hypertension. Most of the compounds in the present **repertoire** of potent NT inhibitors do not meet the requisite pharmacological profiles for successful clinical application, which calls for the discovery of better inhibitors. Advances are being made in the molecular cloning and functional expression of nucleoside transporters that augur well for future drug design efforts.

L169 ANSWER 26 OF 41 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.  
ACCESSION NUMBER: 1996:26043579 BIOTECHNO  
TITLE: Precision 96-**channel** dispenser for  
microchemical techniques  
AUTHOR: Stanchfield J.; Wright D.; Hsu S.; Lamsa M.; Robbins  
A.  
CORPORATE SOURCE: Robbins Scientific Corporation, 814 San Aleso  
Avenue, Sunnyvale, CA 94086, United States.  
SOURCE: BioTechniques, (1996), 20/2 (292-296)  
CODEN: BTNQDO ISSN: 0736-6205  
DOCUMENT TYPE: Journal; Article  
COUNTRY: United States  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB A new automated 96-**channel** microdispenser is described for precise, high- speed dispensing of microliter volumes of reagents. The Hydra-96(TM) is a programmable instrument composed of 96 glass syringes **arrayed** in a microplate format that fills and dispenses in unison under computer control. Studies show the instrument has less than a 2% coefficient of variation (CV) across the syringe **array** when dispensing between 0.5 and 20.0 .mu.L of reagent. Blot hybridization studies demonstrate a simple rinsing protocol using 2% bleach that efficiently cleans the system of DNA without affecting subsequent PCRs. Current uses of the instrument in assembling microassays used in large-scale genetic mapping and sequencing projects and compound

library screening are discussed.

L169 ANSWER 27 OF 41 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.  
ACCESSION NUMBER: 1993:23317703 BIOTECHNO  
TITLE: Ex vivo clonotype primer-directed gene amplification  
to identify malignant T cell **repertoires**  
AUTHOR: Beers T.; Du T.-L.; Rickert M.; Overturf P.; Choi Y.;  
Greenberg S.J.  
CORPORATE SOURCE: Department of Neurology, Roswell Park Cancer  
Institute, Elm and Carlton Streets, Buffalo, NY 14263,  
United States.  
SOURCE: Journal of Leukocyte Biology, (1993), 54/4 (343-350)  
CODEN: JLBIE7 ISSN: 0741-5400  
DOCUMENT TYPE: Journal; Article  
COUNTRY: United States  
LANGUAGE: English  
SUMMARY LANGUAGE: English

AB A novel strategy that utilizes input genomic DNA and overcomes  
limitations encountered with traditional RNA reverse transcription-  
polymerase chain reaction (PCR) amplification methodology is described to  
screen for T cell receptor (TCR) **repertoires**. The methodology  
has been developed to identify individual T cell clonotypes with regard  
to their unique receptor beta chain variable/diversity/joining (VDJ)  
region gene rearrangement. The technique avoids preselection for a given  
antigen specificity and is therefore independent of artificial bias  
introduced by in vitro cell population expansion. This technique was used  
to detect and identify genetically of malignant clones from heterogeneous  
mononuclear cell populations from an **array** of  
hemato-oncological disorders, including mycosis fungoides/Sézary  
Syndrome, adult T cell leukemia, and large granular lymphoproliferative  
disease. An initial primary PCR, directed by a TCR-J.beta. generic primer  
and a complement of family-specific TCR-V.beta. primers, defines  
predominant T cell receptor variable gene usage. Use of a TCR-J.beta.  
generic primer supplants the use of a constant region primer anchor and  
thus eliminates the need to target mRNA. The process of variable gene  
screening also expedites gene sequencing. By sequencing through the VDJ  
**juxtaposed** region, i.e., the third complementarity determinant  
region, clonotype-specific primers are developed and used in a secondary  
clonotype primer-directed PCR (CPD-PCR) to detect, with extreme  
sensitivity and specificity, unique T cell clonal **repertoires**.  
Analysis of the products of the CPD-PCR permits the detection of a single  
malignant cell among one million polyclonal cells and supercedes the  
constraints of prior studies that provide a limited evaluation of family  
variable gene **repertoire** usage. This strategy may be applied in  
the detection of minimal residual disease, in surveillance after  
induction of disease-free states, and in analyzing the effectiveness of  
purging autologous bone marrow of malignant clones.

L169 ANSWER 28 OF 41 BIOTECHNO COPYRIGHT 2002 Elsevier Science B.V.  
ACCESSION NUMBER: 1985:15236344 BIOTECHNO  
TITLE: Unit activity, evoked potentials and slow waves in the  
rat hippocampus and olfactory bulb recorded with a 24-  
**channel** microelectrode  
AUTHOR: Kuperstein M.; Eichenbaum H.  
CORPORATE SOURCE: Department of Biological Sciences, Wellesley College,  
Wellesley, MA 02181, United States.  
SOURCE: Neuroscience, (1985), 15/3 (703-712)  
CODEN: NRSCDN  
DOCUMENT TYPE: Journal; Article  
COUNTRY: United Kingdom  
LANGUAGE: English

AB Activity from a number of neighboring neurons can be recorded  
simultaneously with multichannel microelectrodes. A new version of a 24-



**channel** microelectrode system has been fabricated and used to record different types of neurophysiological data in the rat brain. The system called PRONG (Parallel Recording Of Neural Groups) includes a microelectrode, a lightweight reusable connector, a 24-**channel** FET-hybrid preamplifier, a 3-band 24-**channel** amplifier, a 24-**channel** spike monitor, high-speed digital and analog interfaces and a computer. The electrode-recording locations are arranged in 2 **arrays** of 12 sites. The **arrays** are spaced 100 .mu.m apart along either edge of the recording section and the sites within each **array** are spaced 120 .mu.m apart. The electrodes are fabricated using photolithography in patterned layers totaling 17 .mu.m thick and 114 .mu.m wide in the recording section. The recording sites are 20 .mu.m.sup.2 and are plated with platinum black. Performance of the PRONG was compared with that of conventional single microelectrodes and with results in the literature on three kinds of extracellular activity in the rat hippocampal formation and olfactory bulb: (1) action potentials, (2) evoked field potentials and (3) slow-wave activity. The selectivity and sensitivity of the PRONG compared favorably with characteristics of conventional electrodes. Background noise averaged 15 .mu.V and no signal cross talk was observed between neighboring **channels**. Discriminable action potentials (signal-to-noise ratios of 2:1 to 15:1) were observed at 37-95% of the viable recording sites with a maximum of 19 units in one recording. Units were observed in waking animals for up to 4 days. The waveforms, firing **repertoires** and laminar distribution of units were the same as those recorded with conventional microelectrodes. This indicates that penetration by the PRONG spares tissue from functional damage. 'Instant' laminar profiles were created for commissural and perforant path evoked potentials in the hippocampal formation. These profiles were nearly identical with those created by successive recordings made with conventional microelectrodes. Laminar profiles and behavioral correlates of the hippocampal theta rhythm corresponded to those reported in the literature. Thus neural activity appeared to be 'normal' as collected with this electrode. These results set the foundation for use of the PRONG as a tool for the study of local neural interactions.

L169 ANSWER 29 OF 41 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI  
ACCESSION NUMBER: 2002-11869 BIOTECHDS

TITLE: New **library** of nucleic acids, proteins and peptides, useful e.g. for cloning or drug screening, comprises **grid** of capillaries, each containing defined number of components;  
DNA **library**, peptide **library** and protein **library** construction for DNA chip preparation and high throughput screening

AUTHOR: FUERSTE J P; ERDMANN V A  
PATENT ASSIGNEE: FUERSTE J P; ERDMANN V A  
PATENT INFO: WO 2002013960 21 Feb 2002  
APPLICATION INFO: WO 2000-DE3067 11 Aug 2000  
PRIORITY INFO: DE 2000-1040857 11 Aug 2000  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
OTHER SOURCE: WPI: 2002-241850 [29]

AB DERWENT ABSTRACT: NOVELTY - A **library** (A) of nucleic acids, proteins or peptides, formed as a two-dimensional, positionally resolved **grid** having **grid** elements (GE), each containing a defined number of components of specified sequence, where GE are formed as capillary cavities with one opening at one end, with parallel cavity axes and uniform density of openings of different cavities arranged in a planar **grid** surface, is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) preparing a nucleic acid (NA) **library** (A') in which there is no communication between fluids applied to different GE; and (2) copying an NA **library**

(A or A'). BIOTECHNOLOGY - Preparation: In method (1), a two-dimensional **grid** is formed from the openings of the cavities and the openings are contacted with different NA-containing solutions so that, by capillarity, a part of the solution enters each BE. The openings are separated from the solution, dried and optionally the entire **grid** subjected to an amplification stage. The concentration of NA in solution and the dimensions of the capillary/openings, relative to the amount of solution used, are controlled so that a mean average number of NA is present in each GE. In method (2), all or part of an NA-loaded **grid** and all or part of an empty **grid** are bound together in a defined orientation, with respect to the two-dimensional resolution of their openings. Then either optionally NA in the loaded **grid** is mobilized, an amplification solution introduced into both **grids** and the amplification step performed or NA is transferred to the empty **grid**, the two **grids** are separated and optionally (before or after separation), NA is immobilized in the previously empty **grid**. The **grids** are particularly bonded through an intermediate **grid** mesh in which the number of openings is smaller than the number of GE in the loaded **grid**. The procedure may be repeated with, before each repetition, displacement of the mesh and/or at least one of the **grids** in a defined direction. Preferred Process: In use, GE are treated in parallel with reagents and/or potential interacting compounds, which pass through each capillary. To prepare a protein/peptide **library**, the GE of an NA **library** are treated with an expression mixture and expression reaction performed. To produce an NA **library** on a chip, the **grid** surface is contacted with the chip and NA mobilized/transported simultaneously from GE, while maintaining the two-dimensional orientation of the **library**. NA are transported by application of an electrical or magnetic field, by centrifugation and/or by pressure difference. USE - (A) are used for processing (especially cloning and copying but also e.g. chromosome walking, quantitative (reverse transcription) polymerase chain reaction, expression and polymorphism analyses etc.) of nucleic acid (NA) and for studying interactions between molecules (e.g. in high-throughput screening for possible pharmaceuticals) and diagnosis of (mutation-related) physiological defects), also for sequencing of NA, proteins and peptides. (A) that contain NA can also be used to prepare corresponding protein/peptide **libraries** and to make NA **library** chips. ADVANTAGE - The **library** is prepared simply and in GE reactions occur at very high conversion rates, allowing simple amplification. Particularly all GE are treated simultaneously, rather than by the usual, time-consuming sequential method. EXAMPLE - None given in the source material. (91 pages)

L169 ANSWER 30 OF 41 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

ACCESSION NUMBER: 2002-12252 BIOTECHDS

TITLE: Novel polynucleotide encoding head and neck tumor polypeptides, useful in pharmaceutical compositions, e.g. vaccines, for treating head and neck cancers; vector-mediated recombinant metallo protease fusion protein gene transfer and expression in antigen presenting cell, DNA **microarray**, DNA chip and expression profiling for cancer diagnosis and genetherapy

AUTHOR: WANG T; FAN L

PATENT ASSIGNEE: CORIXA CORP

PATENT INFO: WO 2002012329 14 Feb 2002

APPLICATION INFO: WO 2000-US24226 3 Aug 2000

PRIORITY INFO: US 2000-249933 16 Nov 2000

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2002-257467 [30]

AB DERWENT ABSTRACT: NOVELTY - An isolated polynucleotide (I) comprising

sequences (S1) selected from 273 sequences fully defined in the specification, their complements, sequences comprising 20 contiguous residues of S1, sequences that hybridize to S1 under highly stringent conditions, sequences having 75%, preferably 90%, identity to S1, or degenerate variants of S1, is new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated polypeptide (II) comprising a sequence encoded by (I), a sequence having at least 70%, preferably 90%, identity to (I), a sequence (S2) comprising any one of the 41 amino acid sequences fully defined in the specification, sequences having at least 70%, preferably 90%, identity to S2; (2) an expression vector (III) comprising (I) linked to an expression control sequence; (3) a host cell (IV) transformed or transfected with (III); (4) an isolated antibody (Ab) or its antigen-binding fragment, that specifically binds to (II); (5) detecting (M1) the presence of cancer in a patient, by obtaining a biological sample from the patient, contacting the sample with a binding agent that binds (II), detecting in the sample, a polypeptide that binds to the binding agent and comparing the amount of polypeptide to a predetermined cut-off value, and thus determining the presence of cancer in the patient; (6) a fusion protein (V) comprising (II); (7) an oligonucleotide (VI) that hybridizes to S1 under highly stringent conditions; (8) stimulating (M2) and/or expanding T cells specific for a tumor protein, by contacting T cells with (I), (II) or antigen-presenting cells (APC) expressing (I), under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells; (9) an isolated T cell population (VII), comprising T cell obtained by M2; (10) a composition (C) comprising a first component selected from physiologically acceptable carriers and immunostimulants, and a second component selected from (I), (II), Ab, (V), (VII) and antigen-presenting cell expressing (II); (11) a diagnostic kit comprising (VI) or Ab, and a detection reagent comprising a reporter group; and (12) treating head and neck cancer in a patient, by incubating CD4+ and/or CD8+ T cells isolated from a patient with (I), (II) or antigen presenting cells that express (II), such that the T cell proliferate, administering to the patient an effective amount of proliferative T cell, and thus inhibiting the development of cancer in the patient. WIDER DISCLOSURE - Disclosed as new are: (1) removing tumor cells from a biological sample, by contacting the biological sample with T cells that specifically reacts with (II) under conditions and time sufficient to remove the cells expressing the protein from the sample; (2) inhibiting development of cancer in a patient, by treating the patient with the above said treated biological sample; (3) monitoring the progression of cancer in a patient; (4) kits for carrying out the above said diagnostic methods; and (5) fragments and derivatives of (I) and (II). BIOTECHNOLOGY - Preparation: (I) is cloned by standard recombinant methods. ACTIVITY - Cytostatic. No supporting data given. MECHANISM OF ACTION - Vaccine; gene therapy. No supporting data given. USE - (I), including its encoded polypeptide (II), an antibody (Ab) binding to (II), a fusion protein comprising (II) and a T-cell population stimulated by (I) or (II) are useful for stimulating an immune response in a patient and treating head and neck cancer in a patient. An oligonucleotide (VI) that hybridizes to S1 is useful for determining the presence of cancer in a patient, by obtaining a biological sample from the patient, contacting the sample with (VI), detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide, and comparing the amount of polynucleotide that hybridizes to the oligonucleotides to a predetermined cut-off value (claimed). (I) and (II) are useful in pharmaceutical compositions, e.g. vaccines, and other compositions for the diagnosis and treatment of head and neck cancer. ADMINISTRATION - Administration is intracutaneous, intramuscular, intravenous, subcutaneous, intranasal or oral route. Dosage is 25 microg-5 mg/kg of host. EXAMPLE - cDNA sequences from HN-S7 library (head and neck) were amplified by polymerase chain reaction (PCR) from individual colonies. Their mRNA expression profiles in lung tumor, normal lung, and other normal tumor tissues were examined

using cDNA **microarray** technology. In brief, the clones were arrayed onto glass slides as a multiple replicas, with each location corresponding to a unique cDNA clone. Each chip was hybridized with a pair of cDNA probes that were fluorescence-labeled with Cy3 and Cy5 respectively. Typically, 1 microg of polyA+ RNA was used to generate each cDNA probe. After hybridization, the chips were scanned and the fluorescence intensity recorded for both Cy3 and Cy5 **channels**. The reproducibility of the technology was ensured by including duplicated control cDNA elements at different locations. Further validation of the process was indicated in that several differentially expressed genes were identified multiple times in the study, and the expression profiles for these genes were comparable. The ratio of signals 1 to 2 provides a measure of the level of expression of identified sequences in tumor versus normal tissues. For example, for a sequence comprising 211 nucleotides fully defined in the specification, the tumor specific signal was 7 times that of the signal for the normal tissues tested. Additional analyses were performed on lung **microarray** chips containing **sequences from the subtracted library**. One analysis used a criteria of at least 2-fold overexpression in tumors and an average expression in normal tissues at most 0.2. cDNAs for 39 sequences given in the specification were from subtracted cDNA **library** HN-S7 and were analyzed on lung chip 6 using squamous tumor probes. Full-length cDNA (comprising 1804 nucleotides fully defined in the specification) and protein sequence (comprising 477 amino acids fully defined in the specification) for clone 54707 were also disclosed. Full-length sequence was obtained for clone 55040 (partial sequence comprising 186 nucleotides fully defined in the specification). The full-length DNA sequence comprises 1778 nucleotides fully defined in the specification and the predicted amino acid sequence comprises 470 amino acids fully defined in the specification. The clone was overexpressed in head and neck squamous tumors, and also in lung squamous tumors. The amino acid sequence indicated that the protein is a human metalloproteinase. (200 pages)

L169 ANSWER 31 OF 41 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

ACCESSION NUMBER: 2002-10610 BIOTECHDS

TITLE: Methods for detecting one or more non-nucleic acid analytes using fusion polypeptides with specificity for the analyte, where the polypeptide comprises first and second inactive functional domains and an analyte binding domain; enzyme electrode, biosensor, DNA **array** and high throughput screening, useful for diagnosis

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PATENT ASSIGNEE: MAXYGEN INC

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OTHER SOURCE: WPI: 2002-206219 [26]

AB DERWENT ABSTRACT: NOVELTY - Methods for detecting one or more non-nucleic acid analyte (NAA) using fusion polypeptides with specificity for the analyte, where the polypeptide comprises a first inactive functional domain, an analyte binding domain and a second inactive functional domain, are new. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (1) a method (M1) for detecting one or more NAA, comprising: (a) providing at least one fusion polypeptide (P1) with specificity for a NAA, where P1 comprises a first inactive functional domain, an analyte binding domain, and a second inactive functional domain, where binding of the NAA results in a conformational change which brings the first inactive functional domain and the second inactive functional domain into proximity, therefore converting the first and second inactive functional domains into an optically detectable

functional domain; (b) contacting P1 with a sample comprising the NAA; and (c) detecting the conformational change induced by binding of the NAA, where the NAA is selected from a small organic molecule, a peptide, a polypeptide and a dissolved gas; (2) another method (M2) for detecting one or more NAA, comprising: (a) step (a) of M1, where the first and second inactive functional domains are converted into a catalytic functional domain; (b) providing a substrate for the catalytic functional domain; (c) contacting the fusion polypeptide with a sample comprising the analyte; and (d) detecting the conversion of the substrate to a product; (3) another method (M3) for detecting one or more NAA, comprising: (a) providing at least one polypeptide with specificity for a NAA, where the polypeptide comprises an analyte binding domain and a catalytic domain, where binding of the analyte results in an allosteric conformational change which activates the catalytic domain resulting in conversion of a substrate to a detectable product; and (b) providing a substrate for the catalytic domain; (c) contacting the polypeptide with a sample comprising the analyte; and (d) detecting the product produced by activity of the catalytic domain on the substrate; (4) a method (M4) for detecting an analyte, comprising providing at least one biopolymer which undergoes a conformational change upon binding to an analyte, contacting a sample comprising the analyte to the biopolymer; and detecting the conformation change induced by binding of the analyte, where the analyte is not an ion; (5) a method (M5) for identifying a physiologic state, comprising providing at least one biopolymer which biopolymer undergoes a conformational change upon binding to a marker associated with a physiologic state, contacting the biopolymer with a biological sample comprising the marker, and detecting the conformation change induced by binding of the marker, thereby identifying the physiologic state associated with the marker; (6) a biosensor comprising: (a) a support; and (b) at least one polypeptide with specificity for a NAA, where the polypeptide comprises an analyte binding domain and a catalytic domain, where binding of the analyte results in an allosteric conformational change which activates the catalytic domain resulting in conversion of a substrate to a detectable product, where the polypeptide is immobilized on the support; or (c) at least one fusion polypeptide with specificity for a NAA, where the polypeptide comprises a first inactive functional domain, and analyte binding domain, and a second inactive functional domain, where binding of the analyte brings the first inactive functional domain and the second inactive functional domain into proximity, thereby converting the first and second inactive functional domains into a functional catalytic or optically detectable domain where the fusion polypeptide is immobilized on the support; or (d) a polypeptides immobilized on the solid support, where the polypeptides having different analyte binding specificities, and a detection system; (7) a method (M6) of sensing one or more test stimulus, comprising: (a) providing a **library** of biopolymers comprising nucleic acid variants or expression products of the nucleic acid variants; (b) arraying the **library** in a spatial or logical format to provide a physical or logical **array**; (c) contacting one or more calibrating stimulus to the **array**, where one or more members of the **array** produce one or more detectable signals in response to contact by the one or more calibrating stimulus, thereby producing a calibrating **array** pattern which identifies contact of the **array** by the one or more calibrating stimulus; (d) contacting at least one test stimulus to the **array**, thereby producing a test stimulus **array** pattern; and (e) comparing the test stimulus **array** pattern to the calibrating **array** pattern, thereby identifying the test stimulus; (8) a method (M7) of using a re-usable **array** of biopolymers, comprising: (a) providing a physical or logical **array** of biopolymers comprising nucleic acid variants or expression products of the nucleic acid variants; (b) contacting the physical or logical **array** with one or more first stimulus; (c) observing a first resulting response of the **array**, or

collecting a first product resulting from contact between the **array** and the first stimulus; (d) reusing the **array** by contacting the **array** a second time with the first stimulus, or with a second stimulus, and observing a second resulting response of the **array**, or collecting a second product resulting from contact between the **array** and the first or second stimulus, and, optionally, comparing the first resulting response of the **array** to the second resulting response of the **array**; (9) biopolymer **array** produced by M6 or M7; and (10) a computer comprising a data set corresponding to the labeling biopolymer sensor **array** pattern or test biopolymer sensor **array** pattern of M6 or M7.

BIOTECHNOLOGY - Preferred Method: In M1, the first and second inactive functional domains are derived from a green fluorescent protein or a green fluorescent protein homologue. M1 comprises detecting an electrochemical signal produced by binding of the analyte or detecting an optical signal produced by binding of the analyte. The optical signal is detected by one or more of: ultraviolet spectrophotometry, visible light spectrophotometry, surface plasmon resonance; calorimetry, fluorescence polarization; fluorescence quenching; colorimetric quenching; fluorescence wavelength shift; fluorescence resonance energy transfer (FRET); enzyme linked immunosorbent assay (ELISA) or liquid crystal displays (LCD). The optical signal is produced by displacement of a tethered substrate upon binding of the analyte. The tethered substrate is an analyte analogue. In M2, the conversion of the substrate to a product is detected by detecting an electrochemical signal or an optical signal which is detected as described above. M1, M2, M3, M4 and M5 comprise providing a physical or logical **array** comprising polypeptides which have different analyte binding specificities. In M1, M2, M4 and M5, the polypeptides provide a common signal. The NAA comprises a small molecule, a hormone or a metabolite. The sample is a biological sample (blood, plasma, urine, sweat, cerebrospinal fluid and tears) or an environmental sample. In M3, the conversion of the substrate to product produces an electrochemical signal or an optical signal which is detected as described above. In M3, the conversion of substrate to product by the analyte-bound polypeptides is detected by detecting a common signal. The sample is a biological sample, an environmental sample, or an industrial sample. The sample further comprises an agonist or an antagonist. The analyte comprises a small molecule, a hormone, a metabolite, an ion, an antigen or a ligand. In M4, the biopolymer comprises a polypeptide which comprises an antibody or a receptor. The conformation change results in generation of an optical signal which is detected as described above. The optical signal is produced by displacement of a tethered substrate upon binding of the analyte. The tethered substrate is an analyte analogue. In M5, the biopolymer comprises a polypeptide which comprises an enzyme, an antibody, a receptor or a fusion protein. Preferably the polypeptide is P1, where binding of the analyte results in a conformational change which brings the first inactive functional domain and the second inactive functional domain into proximity, thereby converting the first and second inactive functional domains into a functional catalytic or fluorescent domain. The conformation change results in generation of an optical signal which is detected as described above. The optical signal is produced by displacement of a tethered substrate upon binding of the analyte. The tethered substrate is an analyte analogue. In M6 and M7, the biopolymer **library** comprises or is encoded by recursively recombined nucleic acids. The biopolymer **library** comprises or is encoded by artificially mutated or artificially shuffled nucleic acids. Alternatively, the biopolymer **library** comprises or is encoded by species variants of one or more nucleic acids. Alternatively, the biopolymer **library** comprises or is encoded by nucleic acids produced by recursive recombination of species variants of one or more nucleic acids. The biopolymer **library** comprises photoactivatable members. The method comprises masking a portion of the **array** and exposing the resulting masked **array** to light.

The **array** comprises one or more of a conductive member, a capacitive member, an optically responsive member, an electrically responsive member, and an electrically or logically gated or gateable member. Alternatively, the **array** comprises one or more of: a bio-laser, a polychromic display, a molecular poster, a bar code, a protein TV, a molecular camera, a UV (ultra-violet) molecular camera, an IR (infra-red) molecular camera, or a flat screen display. The **array** members comprise one or more proteins. The proteins comprise electrically conductive proteins. The proteins are purified. The proteins comprise one or more purification tags such as His tags, and FLAG tags. Arraying the biopolymer **library** comprises: (a) arranging the members of the **library** in a logically accessible format; (b) arranging the members of the **library** in a physically **grided** format; (c) plating the members of the **library** in microtiter trays; or (d) arranging the members of the **library** for parallel examination. Arraying the biopolymer **library** or expression product **library** comprises recording the position of members of the **library** in one or more database, or arranging the members of the **library** for sequential examination. The first, second, test or calibrating stimulus are simultaneously, sequentially or alone contacted to biopolymer **library** members. Contact of the of first, second, test or calibrating stimulus produces a signature for a sample type. The signature is representative of one or more phenomenon selected from a metabolic state of a cell, an operon induction in or by a cell, an induction of cell growth, a proliferation in or caused by a cell, a cancer of a cell or tissue, or organism, apoptosis, cell death, cell cycle, cell or tissue differentiation, tumorigenesis, disease state, drug resistance, drug efficacy, antibiotic spectrum, drug toxicity, gas level, SOx, NOx Alzheimer's disease, infection, presence of viruses, viral infection, bacterial infection, HIV infection, AIDS, serum cholesterol, CHDL (undefined) level, LDL (low density lipoprotein), serum triglyceride level, blood glucose level, ion or gas production or internalization, cytokine receptor expression, antibody-antigen interactions, pregnancy, fertility, fecundity, presence or absence of narcotics or other controlled substances, heart attack, presence or absence of steroids, body temperature, presence of sound waves, taste, scent, food composition, beverage composition, and an environmentally monitored condition. The first, second, test or calibrating stimulus are contacted to **library** members in a microtiter plate or fixed on a solid substrate. Alternatively, the first, second, test or calibrating stimulus are contacted to **library** members, or their expression products, fixed on a solid substrate, where the solid substrate comprises a Nickel-NTA coated surface, a silane-treated surface, a pegylated surface, or a treated surface. The biopolymer **library** members or expression products thereof are fixed to an organizational matrix in spatially addressable locations. Alternatively, the first, second, test or calibrating stimulus are contacted to biopolymer **library** members, where member types are fixed on the surface of one or more beads. One or more beads each comprise more than one detectable feature. More than one detectable feature includes a first feature which identifies binding by the first, second, test or calibrating stimulus and a second feature which identifies either the type of bead or the type of **library** member or expression product thereof which is bound to the bead. The first stimulus, the second stimulus, the calibrating stimulus or the test stimulus, is selected from light, radiation, an atom, an ion, and a molecule. The first, second, test or calibrating stimulus comprises, hybridizes to, binds, acts upon or is acted upon by one or more of: radiation, a polymer, a chemical group, a biopolymer, a nucleic acid, an RNA, a DNA, a protein, a ligand, an enzyme, a chemo-specific enzyme, a regio-specific enzyme, a stereo-specific enzyme, a nuclease, a restriction enzyme, an restriction enzyme which recognizes a triplet repeat, a restriction enzyme that recognizes DNA

superstructure, a restriction enzyme with an 8 base recognition sequence, an enzyme substrate, a regio-specific enzyme substrate, a stereo-specific enzyme substrate, a ligase, a thermostable ligase, a polymerase, a thermostable polymerase, a co-factor, a lipase, a protease, a glycosidase, a toxin, a contaminant, a metal, a heavy metal, an immunogen, an antibody, a disease marker, a cell, a tumor cell, a tissue-type, cerebrospinal fluid, a cytokine, a receptor, a chemical agent, a biological agent, a fragrance, a pheromone, a hormone, an olfactory protein, a metabolite, a molecular camera protein, a rod protein, a cone protein, a light-sensitive protein, a lipid, a pegylated material, an adhesion amplifier, a drug, a potential drug, a lead compound, a protein allele, an oxidase, a reductase, or a catalyst. The first, second, test or calibrating stimulus are contacted to the members of the **library** by incubating a solution comprising the test molecule or the calibrating molecule with the **library** members. The solution is a fluid, a polymer solution or a gel. Comparison of the test **array** pattern and the calibrating **array** pattern, or of the first resulting response of the **array** and the second resulting response of the **array**, is performed by a computer. The first, second, test or calibrating stimuli are contacted to the **array** to produce resulting **array** patterns. The methods further comprise recording the resulting **array** patterns in one or more databases, and assigning a bar code to each resulting **array** pattern. The test **array** pattern, the calibrating **array** pattern, the first resulting response of the **array**, or the second resulting response of the **array**, comprises variations in the presence or absence of signal at different locations on or in the **array**. The test **array** pattern, the calibrating **array** pattern, the first resulting response of the **array**, or the second resulting response of the **array** comprises variations in the level of signal at different locations on the **array**. The test **array** pattern, the calibrating **array** pattern, the first resulting response of the **array**, or the second resulting response of the **array** comprises variations in the presence and intensity of signal at different locations on the **array**. An intensity of the test **array** pattern, the calibrating **array** pattern, the first resulting response of the **array**, or the second resulting response of the **array** comprises is measured to quantify the first, second, test or calibrating stimulus. The test **array** pattern, the calibrating **array** pattern, the first resulting response of the **array**, or the second resulting response of the **array** comprises one or more fluorophore emission, photon emission, chemiluminescent emission, coupled luminescent/fluorescent emission or quenching, or detection of one or more fluorophore emission. The test **array** pattern, the calibrating **array** pattern, the first resulting response of the **array**, or the second resulting response of the **array** comprises an electrochemically detectable signal, an amperometrically detectable signal, a potentiometrically detectable signal, a signal detectable as a change in pH, a signal based on specific ion levels, a signal based on changes in conductivity, a piezoelectric signal, a change in resonance frequency, a signal detectable as surface acoustic waves, or a signal detectable by quartz crystal microbalances. The test **array** pattern, the calibrating **array** pattern, the first resulting response of the **array**, or the second resulting response of the **array** comprises multiple wavelengths of light. The test **array** pattern, the calibrating **array** pattern, the first resulting response of the **array** or the second resulting response of the **array** is generated by detection of one or more of: light, H<sub>2</sub>O<sub>2</sub>, glucose oxidase, NADP, NADPH<sup>+</sup>, NAD(P)H reductase, a change in reduction potential, a change in protein conformation, a change in intrinsic fluorescence, fluorescence, luminescence, FRET, absorption, surface plasmon resonance,



antigen binding, antibody binding, enzyme activity, opening of an ion channel, or label binding. At least one member of the biopolymer **library**, or an expression product thereof, is selected, prior to the arraying step, for one or more of: enhanced stability, orientation of protein binding, improved production, cost of manufacture, optimal activity of expressed members which comprise a tag, overexpression mutations, optimized protein folding, permanent enzyme secretion, improved operators, improved ribosome binding sites, avidity, selectivity, production of a detectable side product, and detection limit. The test **array** pattern, the calibrating **array** pattern, the first resulting response of the **array** or the second resulting response of the **array** are detected by one or more of: a microscope, a CCD, a phototube, a photodiode, an LCD (liquid crystal display), a scintillation counter, film, or visual inspection. The test **array** pattern, the calibrating **array** pattern, the first resulting response of the **array** or the second resulting response of the **array** are digitized and stored in one or more database in one or more computer. M6 and M7 further comprise contacting at least one additional stimulus to the **array**, and comparing a resulting additional test stimulus **array** pattern to the calibrating **array** pattern, thereby identifying the at least one additional stimulus, or observing an additional resulting response of the **array**, or collecting an additional product resulting from contact between the **array** and the additional or a previous stimulus, and optionally comparing the additional resulting response to any one or more previous responses of the **array**. The method comprises contacting the **array** with 2, preferably 10, or more additional stimuli. Preferred Biosensor: The biosensor further comprising a conductive element or an optically detectable element. The polypeptides are immobilized with an immobilization matrix selected from carbon paste and a non-biological polymeric matrix. The biosensor further comprises a display. Preferred Biopolymer **Array**: The biopolymer **array** is stable for at least one year under pre-selected storage conditions. USE - The methods and biosensors are useful for detecting a wide range of biological, chemical and biochemical stimuli, e.g. polypeptides, hormones, metabolite and small molecules. They are useful in medical, environmental and industrial diagnostic procedures, for e.g. the **array** can be used for detection of protein biomarkers associated with disease or other physiological condition. EXAMPLE - Regardless of the format of the **library array**, calibration and standardization is performed by exposing the **array** components to one or more known standard, e.g., calibrating or pattern forming, stimulus. For example, to standardize and calibrate the **array** for detection of small organic molecules, the **array** is contacted with known organic molecules, e.g., phenol, toluene, xlenol, and selected derivatives. The resulting response, e.g., luciferase or GFP (green fluorescent protein) activity, or calibrating **array** pattern, is detected and recorded, for example, by a CCD camera or other photoelectric device. The **array** is then exposed to one or more test stimulus. In the case of cultures, this can be accomplished by exposing replicate cultures to one or more test compounds, while in the case of proteins arrayed on a chip, this is best accomplished by washing under conditions amenable to preservation of the **array**, followed by subsequent exposure to the test compounds. Alternative formats for performing detection assays, e.g., on microfluidic devices (e.g., LabMicrofluidic device (RTM) high throughput screening system (HTS) by Caliper Technologies, Mountain View, CA or the HP/Agilent technologies Bioanalyzer using LabChip (TM) technology by Caliper Technologies Corp. See, also, [www.calipertech.com](http://www.calipertech.com)) are available and favorably employed in the context of the present invention. (159 pages)

ACCESSION NUMBER: 2002-06253 BIOTECHDS  
TITLE: Strategy to sequence the genome of *Corynebacterium glutamicum* ATCC 13032: use of a cosmid and a bacterial artificial chromosome **library**; useful for e.g. strain improvement, metabolic engineering, functional genomics and DNA **array**  
AUTHOR: TAUCH A; HOMANN I; MORMANN S; RUBERG S; BILLAULT A; BATHE B; BRAND S; BROCKMANN-GRETZA O; RUCKERT C; SCHISCHKA N; WRENGER C; HOHEISEL J; MOCKEL B; HUTHMACHER K; PFEFFERLE W; PUHLER A; KALINOWSKI M  
CORPORATE SOURCE: Univ Bielefeld; Univ Bielefeld; Univ Bielefeld; Mol Engines Labs; Deutsch Krebsforschungszentrum  
LOCATION: Tauch A, Univ Bielefeld, Zentrum Genomforsch, Univ Str 25, D-33615 Bielefeld, Germany  
SOURCE: JOURNAL OF BIOTECHNOLOGY; (2002) 95, 1, 25-38  
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DOCUMENT TYPE: Journal  
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AB AUTHOR ABSTRACT - The initial strategy of the *Corynebacterium glutamicum* genome project was to sequence overlapping inserts of an ordered cosmid **library**. High-density colony **grids** of approximately 28 genome equivalents were used for the identification of overlapping clones by Southern hybridization. Altogether 18 contiguous genomic segments comprising 95 overlapping cosmids were assembled. Systematic shotgun sequencing of the assembled cosmid set revealed that only 2.84 Mb (86.6%) of the *C. glutamicum* genome were represented by the cosmid library. To obtain a complete genome coverage, a bacterial artificial chromosome (BAC) **library** of the *C. glutamicum* chromosome was constructed in pBeloBAC11 and used for genome mapping. The BAC **library** consists of 3168 BACs and represents a theoretical 63-fold coverage of the *C. glutamicum* genome (3.28 Mb). Southern screening of 2304 BAC clones with PCR-amplified chromosomal markers and subsequent insert terminal sequencing allowed the identification of 119 BACs covering the entire chromosome of *C. glutamicum*. The minimal set representing a 100% genome coverage contains 44 unique BAC clones with an average overlap of 22 kb. A total of 21 BACs represented linking clones between previously sequenced cosmid contigs and provided a valuable tool for completing the genome sequence of *C. glutamicum*. (C) 2002 Elsevier Science B.V. All rights reserved. (14 pages)

L169 ANSWER 33 OF 41 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI

ACCESSION NUMBER: 2002-04931 BIOTECHDS  
TITLE: Immobilizing polypeptides, by contacting them to anchor molecules having nucleophile, so the ester/thioester groups of the polypeptides undergo trans-esterification to attach them to the anchor molecules on the surface; involving vector-mediated gene transfer for expression in host cell, for use in proteomics and high throughput screening  
AUTHOR: NOCK S; SYDOR J  
PATENT ASSIGNEE: ZYOMYX INC  
PATENT INFO: WO 2001098458 27 Dec 2001  
APPLICATION INFO: WO 2000-US19531 19 Jun 2000  
PRIORITY INFO: US 2000-212620 19 Jun 2000  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
OTHER SOURCE: WPI: 2002-114573 [15]

AB DERWENT ABSTRACT: NOVELTY - Immobilizing a polypeptide (I) comprising an ester or thioester (E/T) to a surface, by contacting (I) to an anchor molecule (II) comprising a nucleophilic group (N1) at 2 or 3 position relative to a second nucleophilic group, so the E/T undergoes a trans-esterification reaction with N1 to form an intermediate compound in which (I) is attached to (II) through N1, and attaching (II) to the

surface. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an **array** (A1) of immobilized polypeptides attached to a surface (A1 comprises at least a first polypeptide species and a second polypeptide species and each of the polypeptide species are attached to a separate region of the surface in same orientation, and are folded in a secondary structure as required for a biological activity); (2) an **array** (A2) of immobilized polypeptides attached to a surface which comprises a number of surface regions (each surface region has attached to a polypeptide species and a polynucleotide that encodes the polypeptide species); (3) screening (M1) a **library** of nucleic acids to identify a nucleic acids that encodes a polypeptide having a desired activity, by expressing a number of fusion proteins, each of which is encoded by an expression cassette that comprises a member of the **library** of nucleic acids, an intein coding region, and an open reading frame that encodes a polypeptide that is displayed on a surface of a replicable genetic package (the fusion proteins are displayed on the surface of a replicable genetic package) and screening the replicable genetic packages to identify those that display a polypeptide having the desired activity; (4) a nucleic acid (III) that comprises an expression cassette, comprising an insertion site at which a polynucleotide can be introduced into the expression cassette, an intein coding region (the carboxy terminus of the intein coding region is mutated so that it does not function as a splice junction for intein-mediated cleavage), and an open reading frame that encodes a polypeptide that is displayed on a surface of a replicable genetic package (the introduction of a polynucleotide at the insertion site results in an open reading frame that encodes a fusion protein which comprises a polypeptide encoded by the polynucleotide) which polypeptide is attached at its carboxyl terminus to an amino terminus of the intein, and the surface-displayed polypeptide is attached to the carboxy terminus of the intein; and (5) a kit for use in immobilizing one or more polypeptides containing E/T to a surface of a substrate, comprising an anchor molecule reagent for adapting E/T containing polypeptide to the surface. WIDER DISCLOSURE - The following are also disclosed: (1) expression cassettes and expression vectors that facilitates the use of display on replicable genetic packages for initial screening, followed by intein-mediated derivatization of the polypeptide; (2) synthesizing **arrays** comprising (I); (3) biosensors, micromachined devices, and diagnostic devices that comprise the polypeptide **arrays**; and (4) transferring a target molecule to a reaction chamber, provides solution or condition that dissociates the target molecule from the affinity molecule. BIOTECHNOLOGY - Preferred Method: The intermediate compound undergoes an intramolecular rearrangement in which the second nucleophilic group (N2) on (II) displaces N1, therefore forming a more stable bond between (II) and (I). In M1, the polypeptide encoded by the **library** member is released from the fusion protein by contacting the phage with a nucleophilic compound, which becomes attached to the polypeptide. The nucleophilic compound comprises a compound having N1 and N2. The nucleophilic compound is a 2-aminonucleophile or a 3-aminonucleophile or an aminothiols or a 3-aminothiols, and comprises a thiol or a hydroxyl. Preferred Molecule: (I) comprises a thioester. (II) comprises a 2-aminonucleophile e.g. 2-aminothiol or 3-aminonucleophile. (II) comprises a structure (S1) or (S2), and is attached to the surface prior to or after contacting (I). (II) comprises a functional group that can be covalently linked to a molecule that is attached to the surface, where the function group is selected from ketone, diketone, olefin, epoxide, aldehyde, reactive ester, isocyanate, thioisocyanate, carboxylic acid chloride, disulfide, sulfonate ester, maleimide, isomaleimide, N-hydroxysuccinimide, nitrilotriacetic acid, activated hydroxyl, haloacetyl, activated carboxyl, hydrazide, epoxy, aziridine, sulfonylchloride, acyl hydrazine, trifluoromethyldiaziridine, pyridyldisulfide, N-acyl-imidazole, imidazolecarbamate, vinylsulfone, succinimidylcarbonate, arylazide, anhydride, diazoacetate, benzophenone,

isothiocyanate, isocyanate, imidoester, aminooxy or fluorobenzene. (II) comprises a tag group that can be non-covalently bound to a molecule that is attached to the surface. The tag comprises a binding domain derived from glutathione-S-transferase (GST), streptavidin or green-fluorescent protein (GFP). The tag comprises a peptide that comprises an amino-terminal Cys, Thr or Ser. (I) comprises a non-natural amino acid, and E/T is chemically introduced onto (I) by chemical synthesis of the polypeptide. (I) is obtained by expressing a chimeric gene that encodes a fusion protein and contacting the fusion protein with a nucleophilic compound which releases the polypeptide from the intein at the splice junction and forms (I). The fusion protein comprises the polypeptide and an intein, or its functional portion, which is joined to the polypeptide at a splice junction at the amino terminus of the intein, where the carboxyl terminus of the intein lacks a functional splice junction. The nucleophilic compound is the anchor molecule and comprises a peptide. The peptide comprises a serine, threonine or cysteine at its amino terminus, the oxygen and sulfur of which are the nucleophilic groups that undergo the transesterification reaction. The nucleophilic compound comprises a thiol as the nucleophile. The intein is an Int-n of a split intein and (II) comprises an amino acid sequence that comprises an Int-c of a split intein, where the Int-n and Int-c undergo an intein splicing reaction, therefore attaching (II) to (I). Int-n is derived from a dnaE-n gene and the Int-c is derived from a dnaE-c gene. The dnaE-n gene and dnaE-c gene are from a cyanobacterium species e.g. *Synechocystis* sp.. The fusion protein is expressed in vitro or in vivo by introducing the chimeric gene into a host cell and incubating the host cell under conditions conducive to expression of the fusion protein. The surface on which (I) is immobilized, comprises a **biochip** comprising a non-sample surface and a number of sample portions that are elevated with respect to the non-sample surface, and each sample portion has attached to a single polypeptide species. The **biochip** comprises one or more materials selected from silicon, plastic, gold and glass. Alternately, the surface comprises a microparticle, and (I) is placed in contact with the surface using a microvolume dispenser that comprises a body and at least one vertical **channel** defined within the body, the **channel** being defined by at least one passive valve, where an interior surface defining at least one vertical **channel** is hydrophobic. The dispenser comprises a number of vertical **channels** defined within the body and arranged as an **array**. Each of the peptide species in A1, are covalently attached to the surface-bound linker by a 2-aminonucleophile ester bond e.g. 2-aminothioester bond, which undergoes an intramolecular rearrangement to form an amide bond. The linker is a non-peptide linker and the C-terminus of each of the polypeptide is attached to the surface. The linker comprises the structure S1 or S2. The expression cassette of (III) further comprises a promoter. (III) is a member of a **library** of polynucleotides such as **library** of cDNA molecules, genomic DNA fragments or recombination products. (II) comprises a NH<sub>2</sub>-NH-R and an aminooxy group, where R represents (II), E/T reacts with the reactive group, therefore forming a compound comprising (I) attached to (II) through a reactive group. Preferred Kit: The kit further comprises a DNA vector for introducing E/T into the polypeptide, where the vector is adapted to receive a nucleic acid sequence encoding the polypeptide to form a E/T polypeptide expression vector for expressing the polypeptide as an E/T polypeptide. The kit further comprises a chemical agent for introducing E/T into (I), and instructions for instructing a user to carry out the immobilization method using the kit. The kit further comprises a substrate for attaching (II) immobilizing (I), where (II) is supplied attached to the surface of the substrate for later attaching (I) by a user. (I) is supplied with a kit precoupled with (II). USE - The methods are useful for immobilizing polypeptides and for forming **arrays** of polypeptides (claimed). The immobilized polypeptides are useful for proteomics and high-throughput screening. ADVANTAGE - The

immobilized polypeptides are generally in the same orientation, are of full length and biologically active, and can be readily screened for a desired activity. EXAMPLE - None given.(61 pages)

L169 ANSWER 34 OF 41 WPIDS (C) 2002 THOMSON DERWENT  
ACCESSION NUMBER: 2002-636568 [68] WPIDS  
DOC. NO. NON-CPI: N2002-502922  
DOC. NO. CPI: C2002-179602  
TITLE: Biosensor e.g. for proteomics applications, produces resonant grating effect on reflection radiation spectrum when specific substances are immobilized on it and illuminated.  
DERWENT CLASS: B04 D16 S02 **S03** S05 U12 V07 V08  
INVENTOR(S): CUNNINGHAM, B; LI, P; LIN, B; PEPPER, J; PIEN, H; CUNNINGHAM, B T  
PATENT ASSIGNEE(S): (SRUB-N) SRU BIOSYSTEMS LLC  
COUNTRY COUNT: 96  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002061429	A2	20020808	(200268)*	EN	150
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
US 2002127565	A1	20020912	(200268)		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002061429	A2	WO 2001-US45455	20011023
US 2002127565	A1	US 2000-244312P	20001030
	Provisional	US 2001-283314P	20010412
	Provisional	US 2001-303028P	20010703
	Provisional	US 2001-930352	20010815

PRIORITY APPLN. INFO: US 2001-303028P 20010703; US 2000-244312P  
20001030; US 2001-283314P 20010412; US  
2001-930352 20010815

AB WO 200261429 A UPAB: 20021022  
NOVELTY - A biosensor, where a two-dimensional grating made of high refractive index material is held over a substrate, is new. The depth and period of the grating are set less than a wavelength corresponding to a resonant grating effect specific binding substances are immobilized on surface of the grating and is illuminated to produce a resonant grating effect on reflected radiation spectrum.

DETAILED DESCRIPTION - A biosensor having a two-dimensional grating held over a substrate and covered with a low refractive index cover layer, is new. The period of the grating is set as 0.01-1 micron and depth of the grating is 0.001-1 microns. Specific binding substances are arranged in an **array** of distinct location that define **micro array** spot of 50-500 microns and are immobilized by physical adsorption or chemical binding. Alternatively the biosensor made of a sheet material having relief volume diffraction structure on one of its surfaces which is coated with a reflective material, specific binding substances are immobilized on reflective material that reflect a monochromatic light when being illuminated by broad band of optical wavelengths. The specific reflective wavelength results from optical

interference. Alternatively the biosensor uses the two-dimensional grating made of a electrically conductive transparent material coated on one surface of insulator to produce resonant grating effect. The grating comprises repeated pattern of shapes such as square, circles, ellipses, triangles, ovals, trapezoids, sinusoidal waves, rectangles and hexagons or grids. Each grating region has electrically conducting traces being connected to a voltage source. Alternatively the patterns is of concentric rings with thickness of half of grating period and pitch of one grating period greater than inner diameter of previous ring to produce a reflected radiation spectrum independent of illumination polarization angle. The biosensor can also be constructed with an **array** of holes or posts producing similar effects. The biosensor is also constructed with a pair of gratings arranged one above the other.

INDEPENDENT CLAIMS are included for:

- (1) a liquid containing vessel with the biosensor as its internal surface such as a micro titer plate, a test tube, a Petri dish or a microfluidic **channel**;
- (2) a reduction system using the biosensor preferably the reduction system uses a scanning mirror device such as a linear galvanometer operating at a frequency of 2Hz-120Hz operating at mechanical scan angle of 10-20 degrees to reflect laser light of wavelength 780 nm, 785 nm, 810 nm or 830 nm from a laser diode;
- (3) a biosensor composition containing 50-1000 individual biosensors held in a holding picture, the size of the biosensors are 1-5 mm<sup>2</sup> and are arranged at 25-1000 distinct locations, the biosensors can be fabricated or placed on tip of a multi fiber optic probe;
- (4) determining a resonant frequency of binding parameter in resonant reflectance spectrum using a calorimetric biosensor, multiple measurements are done using calorimetric resonant biosensor and reflectance spectra are obtained, a curve is fit using the resonant reflectance data by including inherent noise and the location of maximum peak is obtained from the fit curve, the maximum resonant peak identifies amount of bimolecular asterisk binding;
- (5) a computer readable medium storing instructions for curve fitting using a processor; and
- (6) detecting **interaction** between test molecules using the novel biosensor.

USE - The biosensor is useful for detecting activity of an enzyme, and for detecting the binding of one or more specific binding substances (e.g. nucleic acids, polypeptides, antigens, polyclonal antibodies, monoclonal antibodies, single chain antibodies, F(Ab) fragments, F(ab')<sub>2</sub> fragments, Fv fragments, small organic molecules, cells, viruses, bacteria and biological samples in biological samples (including blood, plasma, serum, gastrointestinal secretions, homogenates of tissues or tumors, synovial fluid, feces, saliva, sputum, cyst fluid, amniotic fluid, cerebrospinal fluid, peritoneal fluid, lung lavage fluid, semen, lymphatic fluid, tears and prostatic fluid). The biosensor is also useful for measuring the amount of one or more binding partners in a test sample, immobilizing specific binding substances onto the biosensor, and for detecting an **interaction** of a **first** molecule with a **second** test molecule. The biosensor composition is useful for detecting binding of specific binding substances to their respective binding partners in vivo. (All claimed). The biosensor is also useful for detecting biomolecular **interactions** using optical resonance, for proteomics applications such as for analyzing protein, DNA sequences and PHAGE display **library**.

ADVANTAGE - Enables thousands of individual binding reactions to take place simultaneously on biosensor surface so that large number of bimolecular **interaction** can be measured parallely. Suits high-throughput screening of pharmaceutical compound **library** with protein target, **micro array** screening of protein-protein **interaction**, etc. The biosensor can be manufactured easily using plastic embossing process and hence is

inexpensive. The biosensor can be incorporated in common disposable laboratory **array** platform such as micro titer plates and **micro array** slides.  
Dwg.0/52

L169 ANSWER 35 OF 41 WPIDS (C) 2002 THOMSON DERWENT  
ACCESSION NUMBER: 2002-583487 [62] WPIDS  
DOC. NO. NON-CPI: N2002-462738  
DOC. NO. CPI: C2002-164911  
TITLE: Novel protein **array** useful for detecting the presence of individual proteins in sample, comprises **heavy-chain variable domain antibodies** or **antibody** fragments obtainable from Camelidae.  
DERWENT CLASS: B04 D16 S03  
INVENTOR(S): DE HAARD, J J W; HERMANS, P; LANDA, I; VERRIPS, C T  
PATENT ASSIGNEE(S): (DHAA-I) DE HAARD J J W; (UNIL) HINDUSTAN LEVER LTD; (UNIL) UNILEVER NV; (UNIL) UNILEVER PLC  
COUNTRY COUNT: 98  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
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WO 2002048193	A2	20020620	(200262)*	EN	80
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2002029639	A	20020624	(200267)		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
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WO 2002048193	A2	WO 2001-EP14471	20011203
AU 2002029639	A	AU 2002-29639	20011203

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
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AU 2002029639	A Based on	WO 200248193

PRIORITY APPLN. INFO: EP 2000-311142 20001213

AB WO 200248193 A UPAB: 20020926

NOVELTY - A protein **array** (I) comprising a number of **antibodies** or their fragments, where the **antibodies** or their fragments are comprised of **heavy-chain variable domain antibodies** or **antibody** fragments, obtainable from Camelidae, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an **array** (II) of bound proteins, comprising (I), and a number of different proteins which are expression products or post-translationally modified forms, or fragments of either of these, of a cell or population of cells in an organism, where each of the different proteins is bound to an **antibody** or its fragment on a separate patch or hole of the **array** after substantial removal of abundant proteins that do not provide useful information on the condition of the cell or population of cells investigated;

(2) a diagnostic device (III) comprising (I) or (II);

(3) removing (M1) abundant proteins from an extract or sample which do not provide useful information on the condition of a cell or tissue in the extract or sample to be investigated, involves removing the abundant proteins by affinity chromatography using **heavy-chain variable domain antibodies**, or **antibody** fragments, obtainable from Camelidae;

(4) producing (I) or (II); and

(5) simultaneous processing (M3) target antigens and evaluating selection conditions, by using the combination of panning on a microtiter plate and the predictive value of phage-enzyme linked immunosorbent assay (ELISA), carried out simultaneously.

USE - (I) is useful for assaying in parallel for a number of different proteins in a sample which are expression products, or post-translationally modified forms of such expression products, or fragments of either of these, of a cell or a population of cells in an organism, for determining the protein expression pattern of a cell or a population of cells, for comparing the protein expression patterns of protein extract or tissue A and protein extract or tissue B, or for evaluating a disease condition in a tissue in an organism. M1 is useful for removing abundant proteins from an extract or sample which do not provide useful information on the condition of a cell or tissue in the extract or sample to be investigated.

(M3) is useful for simultaneous processing of target antigens and evaluating selection conditions (claimed). (I) is useful for detecting the presence of individual proteins in a sample, comparing the distribution of proteins so revealed in different cell types, and identification of proteins that may be of importance in determining the altered properties of cells in disease, aging or other conditions.

ADVANTAGE - (I) is capable of detecting even minor changes in the expression of proteins in cell and tissue extracts and has an optimal signal to noise ratio by removing non-informative abundant proteins from the cell or tissue extracts. (I) allows a direct, and semi-quantitative assessment of the protein content of a given cell type and determines the functional properties of the cell, much more directly than the amounts of different mRNAs that may be present. Further, since proteins are generally much more stable than mRNAs, the results obtainable with (I) is less dependent on the details of the experimental protocol followed. (I) is robust, and can be used several times, with complete removal of bound antigens in between, without loss of quality of the results obtainable. Using a **heavy-chain variable domain** derived from an **immunoglobulin** that is naturally devoid of **light chains** (VHH) in (I) provides a number of advantages, such as an improvement of sensitivity/resolution in the order of 10-100 times, and detection of post-translationally modified proteins.

(M3) enables the simultaneous processing of large numbers of target antigens in a controlled way as well as the evaluation of many application conditions which can be tested for selections. The microtiter plate format allows more conditions to be tested without increasing the effort. The incorporated phage-ELISA generates on-line information about the success or failure of a certain panning condition. This feature combined with the microtiter plate format allows the complete automation of the technology, based on computer-made decisions on the values of the phage-ELISA for continuation of a limited number of selections. In (M3), due to the fact that many different conditions can be tested, varying amounts of input-phages can be used simultaneously in order to decrease the enrichment of sticky phage-**antibodies**. By dilution of input phage, high affinity phage-**antibodies** can compete more effectively with non-specific or low affinity phage-**antibodies**. Hence, the number of bound low-affinity or non-specific phage-**antibodies** will drop relatively faster than the number of the high-affinity **antibodies** when lower numbers of input-phage are used.

Therefore, compared to current panning methods micro-panning is not



only a matter of scaling down, but the key difference in the working principle is that micro-panning is driven by lowering the number of non-specific phage-**antibodies**, whereas current panning methods are focussed on increasing the number of specific ones. Although the final goal is the same the traditional panning method is more susceptible to sticky phage-**antibodies** which can increase during panning and thereby totally drive out the specific ones, especially when used at high tiers. Therefore, micro-panning is an effective tool for selecting both naive, synthetic and immune **libraries** on large numbers of different target molecules, thereby enabling the generation of large panels of **antibodies** in rather short time frames needed for the generation of **arrays** (proteomics). The format of the method allows automation for high throughput panning without the need for sophisticated robotics.

Dwg.0/4

L169 ANSWER 36 OF 41 WPIDS (C) 2002 THOMSON DERWENT  
ACCESSION NUMBER: 2002-241992 [29] WPIDS  
DOC. NO. NON-CPI: N2002-186835  
DOC. NO. CPI: C2002-072885  
TITLE: Composition for identifying monoclonal **antibodies**  
specific for **target** antigens, comprises support  
with **array** of monoclonal **antibodies**  
having unknown specificities for antigens fixed to  
support at **antibody** non-binding region.  
DERWENT CLASS: B04 D16 S03  
INVENTOR(S): HU, Q  
PATENT ASSIGNEE(S): (HUQQ-I) HU Q  
COUNTRY COUNT: 96  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002014866	A2	20020221	(200229)*	EN	17
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
US 2002048823	A1	20020425	(200233)		
AU 2001084899	A	20020225	(200245)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002014866	A2	WO 2001-US25450	20010813
US 2002048823	A1	Provisional	US 2000-224854P 20000811
			US 2001-929874 20010813
AU 2001084899	A		AU 2001-84899 20010813

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001084899	A Based on	WO 200214866

PRIORITY APPLN. INFO: US 2000-224854P 20000811; US 2001-929874  
20010813

AB WO 200214866 A UPAB: 20020508  
NOVELTY - A composition (I) comprising a solid support (S) with  
**array** of several monoclonal **antibodies** (MAbs) or their

binding fragments derived from animals/organisms having unknown specificity for one or more antigens (Ag) e.g., orphan antigen, affixed to (S) at non binding region of MAb or its fragment, leaving binding region to bind Ag upon contact upon contact, where MABs have binding specificities for a number of Ag, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) identifying (M1) a monoclonal **antibody** specific for an orphan antigen for which an **antibody** has not been identified;

(2) profiling (M2) a number of unknown Ag derived from a particular source, comprising contacting 100-500000 monoclonal **antibodies** or its binding fragments having unknown specificity for Ag affixed to (S) with a number of target Ag each having a tag or label for detecting the Ag bound to a monoclonal **antibody** or its fragment, detecting any bound target Ag on (S), and identifying the monoclonal **antibody** or its fragment to which any tagged or labeled target Ag binds;

(3) comparing (M2) profiles of a number of Ag derived from comparable sources;

(4) a kit for identifying a monoclonal **antibody** for a target orphan antigen that has no known monoclonal **antibody**, comprising (I) and instructions for screening a target orphan antigen on (S) comprising MABs; and

(5) a kit for profiling a source comprising a number of orphan antigens by monoclonal **antibody** binding characteristics, comprising (I), reagents for conducting an assay on (S) for profiling the Ag source by monoclonal **antibody** binding, and instructions for conducting the assay.

USE - (I) comprising solid support which has an **array** of monoclonal **antibodies**, is useful for identifying a monoclonal **antibody** specific for an orphan antigen for which an **antibody** has not been identified. It is also useful for profiling a number of unknown Ag derived from a particular source and for comparing profiles of a number of Ag derived from comparable sources (all claimed). The methods are useful for finding a monoclonal **antibody** for an Ag, to characterize Ag from a particular source (e.g. a source comprising an animal having a disease) in order to develop tools for understanding a condition (e.g. the disease) on that source. The methods are also useful for finding a different **antibody** for an Ag which has one or more **antibodies** already, but for which another **antibody** might be desirable to identify.

ADVANTAGE - (I) increases the efficiency, speed and success rate of monoclonal **antibody** identification for a particular target Ag.  
Dwg.0/0

L169 ANSWER 37 OF 41 WPIDS (C) 2002 THOMSON DERWENT  
ACCESSION NUMBER: 2002-206219 [26] WPIDS  
CROSS REFERENCE: 2002-188733 [24]  
DOC. NO. NON-CPI: N2002-157036  
DOC. NO. CPI: C2002-063239  
TITLE: Methods for detecting one or more non-nucleic acid analytes using fusion polypeptides with specificity for the analyte, where the polypeptide comprises **first** and **second** inactive functional **domains** and an analyte binding **domain**.  
DERWENT CLASS: B04 D16 S03  
INVENTOR(S): DAVIS, S C; KREBBER, C; MINSHULL, J; RAILLARD, S A; VOGEL, K; WELCH, M  
PATENT ASSIGNEE(S): (MAXY-N) MAXYGEN INC  
COUNTRY COUNT: 96  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
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WO 2002010750 A2 20020207 (200226)\* EN 159  
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
NL OA PT SD SE SL SZ TR TZ UG ZW  
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU  
SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW  
AU 2001079135 A 20020213 (200238)  
US 2002127623 A1 20020912 (200262)

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WQ 2002010750	A2	WO 2001-US24182	20010731
AU 2001079135	A	AU 2001-79135	20010731
US 2002127623	A1 Provisional	US 2000-222056P	20000731
	Provisional	US 2000-244764P	20001031
		US 2001-920607	20010731

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001079135	A Based on	WO 200210750

PRIORITY APPLN. INFO: US 2000-244764P 20001031; US 2000-222056P  
20000731; US 2001-920607 20010731

AB WO 200210750 A UPAB: 20020926  
NOVELTY - Methods for detecting one or more non-nucleic acid analyte (NAA) using fusion polypeptides with specificity for the analyte, where the polypeptide comprises a **first** inactive functional domain, an analyte binding domain and a **second** inactive functional domain, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

- (1) a method (M1) for detecting one or more NAA, comprising:
  - (a) providing at least one fusion polypeptide (P1) with specificity for a NAA, where P1 comprises a **first** inactive functional domain, an analyte binding domain, and a **second** inactive functional domain, where binding of the NAA results in a conformational change which brings the **first** inactive functional domain and the **second** inactive functional domain into proximity, therefore converting the **first** and **second** inactive functional domains into an optically detectable functional domain;
  - (b) contacting P1 with a sample comprising the NAA; and
  - (c) detecting the conformational change induced by binding of the NAA, where the NAA is selected from a small organic molecule, a peptide, a polypeptide and a dissolved gas;
- (2) another method (M2) for detecting one or more NAA, comprising:
  - (a) step (a) of M1, where the **first** and **second** inactive functional domains are converted into a catalytic functional domain;
  - (b) providing a substrate for the catalytic functional domain;
  - (c) contacting the fusion polypeptide with a sample comprising the analyte; and
  - (d) detecting the conversion of the substrate to a product;
- (3) another method (M3) for detecting one or more NAA, comprising:
  - (a) providing at least one polypeptide with specificity for a NAA, where the polypeptide comprises an analyte binding domain and a catalytic domain, where binding of the analyte results in an allosteric conformational change which activates the catalytic domain resulting in conversion of a substrate to a detectable product; and

- (b) providing a substrate for the catalytic domain;
  - (c) contacting the polypeptide with a sample comprising the analyte;
- and
- (d) detecting the product produced by activity of the catalytic domain on the substrate;
- (4) a method (M4) for detecting an analyte, comprising providing at least one biopolymer which undergoes a conformational change upon binding to an analyte, contacting a sample comprising the analyte to the biopolymer; and detecting the conformation change induced by binding of the analyte, where the analyte is not an ion;
  - (5) a method (M5) for identifying a physiologic state, comprising providing at least one biopolymer which biopolymer undergoes a conformational change upon binding to a marker associated with a physiologic state, contacting the biopolymer with a biological sample comprising the marker, and detecting the conformation change induced by binding of the marker, thereby identifying the physiologic state associated with the marker;
  - (6) a biosensor comprising:
    - (a) a support; and
    - (b) at least one polypeptide with specificity for a NAA, where the polypeptide comprises an analyte binding domain and a catalytic domain, where binding of the analyte results in an allosteric conformational change which activates the catalytic domain resulting in conversion of a substrate to a detectable product, where the polypeptide is immobilized on the support; or
    - (c) at least one fusion polypeptide with specificity for a NAA, where the polypeptide comprises a **first** inactive functional domain, and analyte binding domain, and a **second** inactive functional domain, where binding of the analyte brings the **first** inactive functional domain and the **second** inactive functional domain into proximity, thereby converting the **first** and **second** inactive functional domains into a functional catalytic or optically detectable domain where the fusion polypeptide is immobilized on the support; or
    - (d) a polypeptides immobilized on the solid support, where the polypeptides having different analyte binding specificities, and a detection system;
  - (7) a method (M6) of sensing one or more test stimulus, comprising:
    - (a) providing a **library** of biopolymers comprising nucleic acid variants or expression products of the nucleic acid variants;
    - (b) **arraying** the **library** in a spatial or logical format to provide a physical or logical **array**;
    - (c) contacting one or more calibrating stimulus to the **array**, where one or more members of the **array** produce one or more detectable signals in response to contact by the one or more calibrating stimulus, thereby producing a calibrating **array** pattern which identifies contact of the **array** by the one or more calibrating stimulus;
    - (d) contacting at least one test stimulus to the **array**, thereby producing a test stimulus **array** pattern; and
    - (e) comparing the test stimulus **array** pattern to the calibrating **array** pattern, thereby identifying the test stimulus;
  - (8) a method (M7) of using a re-usable array of biopolymers, comprising:
    - (a) providing a physical or logical array of biopolymers comprising nucleic acid variants or expression products of the nucleic acid variants;
    - (b) contacting the physical or logical array with one or more first stimulus;
    - (c) observing a first resulting response of the array, or collecting a first product resulting from contact between the array and the first stimulus;
    - (d) reusing the array by contacting the array a second time with the

first stimulus, or with a second stimulus, and observing a second resulting response of the array, or collecting a second product resulting from contact between the array and the first or second stimulus, and, optionally, comparing the first resulting response of the array to the second resulting response of the array;

(9) biopolymer array produced by M6 or M7; and

(10) a computer comprising a data set corresponding to the labeling biopolymer sensor array pattern or test biopolymer sensor array pattern of M6 or M7.

USE - The methods and biosensors are useful for detecting a wide range of biological, chemical and biochemical stimuli, e.g. polypeptides, hormones, metabolite and small molecules. They are useful in medical, environmental and industrial diagnostic procedures, for e.g. the array can be used for detection of protein biomarkers associated with disease or other physiological condition.

Dwg.0/7

L169 ANSWER 38 OF 41 WPIDS (C) 2002 THOMSON DERWENT  
ACCESSION NUMBER: 2002-536036 [57] WPIDS  
CROSS REFERENCE: 1998-557527 [47]  
DOC. NO. NON-CPI: N2002-424404  
DOC. NO. CPI: C2002-151944  
TITLE: Microfluidic systems for performing biochemical analysis  
e.g. DNA sequencing, genomic screening, and drug  
screening comprises microfluidic devices for moving and  
mixing small fluid volumes.  
DERWENT CLASS: B04 D16 S03  
INVENTOR(S): BOUSSE, L J; KNAPP, M; KOPF-SILL, A R; PARCE, J W  
PATENT ASSIGNEE(S): (MOUN-N) MOUNTAIN VIEW PHARM INC  
COUNTRY COUNT: 1  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6403338	B1	20020611	(200257)*		61

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 6403338	B1	Provisional	US 1997-86240P 19970404
		CIP of	US 1997-835101 19970404
		Provisional	US 1997-68311P 19971219
		Div ex	US 1998-54962 19980403
			US 2000-605379 20000627

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 6403338	B1 Div ex	US 6235471

PRIORITY APPLN. INFO: US 2000-605379 20000627; US 1997-86240P  
19970404; US 1997-835101 19970404; US  
1997-68311P 19971219; US 1998-54962 19980403

AB US 6403338 B UPAB: 20020906

NOVELTY - A microfluidic system (I), comprising a microfluidic device comprising at least two **intersecting** microscale channels, a storage element (separable from the microfluidic device and comprising a reagent storage substrate and reagent(s)) and a sampling element coupled to the storage element and one of the microscale channels (the reagents comprise at least 70% of all possible oligonucleotides having a length of n nucleotides).

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a system (II) for detecting a sequence of nucleotides in a target nucleic acid sequence, comprising:

(a) a microfluidic device comprising at least a **first** analysis channel and at least a **first** probe introduction channels (the analysis channel **intersects** and is in fluid communication with the probe introduction channel);

(b) a source of the target nucleic acid sequence in fluid communication with the analysis channel;

(c) several separate sources of oligonucleotide probes in fluid communication with the probe introduction channel (each of the several separate sources contains an oligonucleotide probe having a different nucleotide sequence of length n);

(d) a sampling system for separately transporting a volume of each of the oligonucleotide probes from the sources of oligonucleotide probes to the probe introduction channel and injecting each of the oligonucleotide probes into the analysis channel to contact the target nucleic acid sequence; and

(e) a detection system for identifying whether each oligonucleotide probe hybridizes with the target nucleic acid sequence.

USE - (I) Is useful for genotyping a sample material, by flowing a sample comprising a nucleic acid into a microscale chamber or channel in the microscale device, modifying the complexity of the sample in the reaction region of the device to form a modified sample, and detecting several polymorphisms in the modified sample.

The microscale device comprises a main sample channel and one or more parallel analysis channels **intersecting** the main sample channel. Flowing the sample comprises introducing the sample into the main sample channel and aliquoting the sample into the one or more parallel analysis channels. The microscale device comprises 1-500 parallel analysis channels. One or more parallel analysis channels are **intersected** by one or more reagent introduction channel, and further comprise terminal reservoirs opposite the main sample channel. Modifying the complexity of the sample comprises concentrating or purifying one or more subsets of nucleic acid sequences in the sample, amplifying one or more subsets of nucleic acid sequences in the sample using pre-selected primers that flank the subsets of nucleic acid sequences, or hybridizing one or more subsets of nucleic acid sequences in the sample with a predefined probe that is complementary to the subsets of nucleic acid sequences.

Amplification comprises introducing selected primers, dNTPs or ddNTPs into one or more parallel analysis channels. Several polymorphisms are detected by size-based electrophoretic separation, sequencing the amplified sample by Sanger method of oligonucleotide sequencing, or hybridizing the amplified sample to one or more members of an oligonucleotide **array**. Detection comprises digesting the amplified sample with a nuclease to produce fragments, separating the digested fragments by a size-based separation technique to generate a nuclease digestion pattern, and correlating the nuclease digestion pattern to a presence or absence of a particular marker sequence (all claimed).

(I) Is useful for performing a variety of chemical, biochemical and biological and other fluidic operations, including polymerase chain reaction (PCR), DNA sequencing, integrated or sequential screening of chemical or biological **libraries**, purification of molecules of interest.

(I) Has applicability e.g. as metering or dispensing systems in both biological and non-biological application. The microfluidic devices and systems are useful for performing fluid operations that require a large number of iterative fluid manipulations, in a microscale, or sealed and readily automated format.

ADVANTAGE - The system increases the speed and simplicity of screening, manipulating and assessing fluidic reagents, reagent mixtures, reaction products, and permits the performance of fluidic operations without requiring large amounts of space, expensive reagents and/or

equipment, or excessive time and labor costs.  
Dwg.0/23

L169 ANSWER 39 OF 41 WPIDS (C) 2002 THOMSON DERWENT  
ACCESSION NUMBER: 2001-299926 [31] WPIDS  
DOC. NO. NON-CPI: N2001-215196  
DOC. NO. CPI: C2001-092050  
TITLE: Lipid **microarray** device, useful e.g. for  
detecting analytes and for drug screening, comprises a  
substrate with many discrete, individually addressable  
lipid bilayers.  
DERWENT CLASS: A89 B04 D16 J04 S03  
INVENTOR(S): CREMER, P S; SIMANEK, E E; YANG, T  
PATENT ASSIGNEE(S): (TEXA) UNIV TEXAS A & M SYSTEM  
COUNTRY COUNT: 95  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001020330	A1	20010322	(200131)*	EN	86
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001038833	A	20010417	(200140)		
EP 1218745	A1	20020703	(200251)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001020330	A1	WO 2000-US25627	20000918
AU 2001038833	A	AU 2001-38833	20000918
EP 1218745	A1	EP 2000-963609	20000918
		WO 2000-US25627	20000918

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001038833	A Based on	WO 200120330
EP 1218745	A1 Based on	WO 200120330

PRIORITY APPLN. INFO: US 2000-564708 20000504; US 1999-154576P  
19990917

AB WO 200120330 A UPAB: 20010607

NOVELTY - Lipid **microarray** device (A) is new.

DETAILED DESCRIPTION - (A) comprises:

- (1) a substantially planar substrate;
- (2) a plurality of independently addressable isolated lipid bilayers partitioned discreetly upon the substrate;
- (3) at least a **first** aqueous solution disposed upon at least a **first** of the independently addressable partitioned lipid bilayers, where at least a **first** aqueous solution comprises at least a **first** constituent that **interacts** with the lipid bilayer; and
- (4) at least a **second** aqueous solution disposed upon at least a **second** of the independently addressable partitioned lipid bilayers; where at least a **second** aqueous solution

comprises:

(a) the **first** constituent that **interacts** with the lipid bilayer and at least a **second** constituent that binds to the **first** constituent or to the lipid bilayer; or

(b) a **second** distinct constituent that **interacts** with the lipid bilayer.

INDEPENDENT CLAIMS are also included for the following:

(a) apparatus comprising (A) and a robotic device for spatially addressing each individual LBL;

(b) apparatus comprising several (A);

(c) apparatus for constructing (A);

(d) apparatus for depositing aqueous solutions on selected LBL;

(e) apparatus for detecting a target in an aqueous sample in contact with an LBL; and

(f) identifying, from a population of aqueous solutions, a constituent that (in)directly **interacts** with at least one component of an LBL.

USE - The device is used for detecting (as biosensor) or selecting targets (e.g. pharmaceuticals, pathogenic microorganisms, nucleic acids, proteins etc.) that **interact** with components of LBL, e.g. for genomics, drug screening, studying the molecular basis of disease, detecting antibodies etc.

ADVANTAGE - Thousands of distinct LBL can be produced on a single **biochip** and the confined aqueous phases above LBL facilitate reagent delivery/removal, probing etc., so provide a high throughput screening system. The system allows simultaneous measurements of polyvalent surface adsorption under physiological flow conditions.  
Dwg.0/9

L169 ANSWER 40 OF 41 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1993-045736 [05] WPIDS

DOC. NO. NON-CPI: N1993-035017

TITLE: Stack loader arrangement for automated **library** system - receives stack of data storage media cartridges from **library** system robot, which are loaded onto tape drive.

DERWENT CLASS: T03

INVENTOR(S): MOY, M E; OSTWALD, T C

PATENT ASSIGNEE(S): (STOS) STORAGE TECHNOLOGY CORP

COUNTRY COUNT: 17

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9301595	A1	19930121	(199305)*	EN	43
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE					
W: AU CA JP					
AU 9222979	A	19930211	(199321)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9301595	A1	WO 1992-US5484	19920630
AU 9222979	A	AU 1992-22979	19920630

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9222979	A Based on	WO 9301595

PRIORITY APPLN. INFO: US 1991-724214 19910701



AB WO 9301595 A UPAB: 19930924

The system has an **array** (201,202) of data storage media cartridge storage locations, a media drive mechanism (211), a stack loader and a robotic transporter (230). The media drive mechanism is connected via a data link (171) to a host computer (101) and is located **juxtaposed** to the **array** (201,202) of data storage media cartridge storage locations.

The media drive mechanism is used to read and/or write data onto the data storage media cartridge which is loaded into the mechanism. The stack loader is attached to the media drive mechanism for automatically storing a number of media cartridges and loading the media cartridges in sequence into the media drive mechanism. The robotic transporter is used to transport the media cartridges between the storage locations and the stack loader.

ADVANTAGE - The automated **library** system, performs the time critical operations before the less time critical operations.  
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L169 ANSWER 41 OF 41 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1986-036850 [06] WPIDS

DOC. NO. NON-CPI: N1986-026894

TITLE: Master slice device with on-chip memory - has conductive lines providing logic levels **intersecting** input line and memory block comprising MIS transistors.

DERWENT CLASS: U11 U13 U14

INVENTOR(S): FUJII, S; TAKAYAMA, Y; TANABE, T

PATENT ASSIGNEE(S): (FUIT) FUJITSU LTD

COUNTRY COUNT: 6

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 170052	A	19860205	(198606)*	EN	35
R: DE FR GB					
JP 61022648	A	19860131	(198611)		
JP 61022649	A	19860131	(198611)		
US 4780846	A	19881025	(198845)		
KR 9000178	B	19900123	(199048)		
EP 170052	B	19920401	(199214)		24
R: DE FR GB					
DE 3585756	G	19920507	(199220)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 170052	A	EP 1985-107918	19850627
JP 61022648	A	JP 1984-135210	19840702
JP 61022649	A	JP 1984-135214	19840702
US 4780846	A	US 1985-750163	19850628
EP 170052	B	EP 1985-107918	19850627

PRIORITY APPLN. INFO: JP 1984-135210 19840702; JP 1984-135214  
19840702

AB EP 170052 A UPAB: 19930922

At least one memory block circuit has a number of input circuits each connected to one of a number of input lines provided to a peripheral portion of the block. The input lines are formed by a conductive layer and a conductive line is provided to the peripheral portion to supply a logic level. A **second**, similar conductive line provides a **second** logic level to the periphery, both lines being formed from a **second** conductive layer.

One of the conductive lines is connected to at least one of the input lines by a contact arrangement which clips the input signal to the selected logic level enabling a change of memory capacity or a function of the memory circuit block. The conductive lines may **intersect** the input line and the memory block may comprise MIS transistors.

ADVANTAGE - Simplifies CAD design by not needing memory wiring.  
Pattern inserted into **library**.

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